THE PHOTOSENSITIZING FURANOCOUMARINS OF *PHEBALIUM ARGENTEUM* (BLISTER BUSH)*

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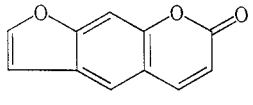
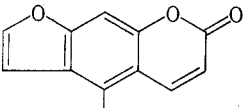
Phebalium argenteum Smith (Rutaceae) occurs[1] throughout the lower south-western area of Western Australia and is a conspicuous undergrowth in the karri forest between Denmark and the Margaret River. It is known locally as "blister bush"; skin contact with the leaves produces painful vesication on exposure to sunlight. Variations in the intensity of the effect have been noted.[2]

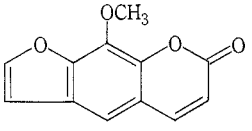
Finlayson[1] showed that, in addition to monoterpenes, sesquiterpenes, and saturated aliphatic ketones, the essential oil of *P. argenteum* contained small amounts of a substance (m.p. 165°) of coumarin-like smell. This compound was later identified[3] as psoralen (I). *Phebalium argenteum* has now been reinvestigated with a view to studying the presence of this and other coumarins.



(I)



(II)



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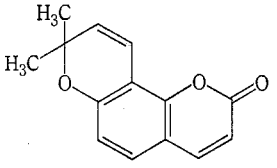

(IV)

Leaves and branchlets of *P. argenteum* collected at Crystal Springs, near Walpole in Western Australia, were air-dried, milled, and successively extracted with light petroleum, ether, and methanol. Only the ether extract showed the intense fluorescence characteristic of substituted coumarins. Its constituents were separated by preparative thin-layer chromatography and afforded pure samples of psoralen (I) (m.p. 164–165°; lit.[4] 161–162°; 0·37%), bergapten (II) (m.p. 189–190°; lit.[5] 187–188°; 0·28%), xanthotoxin (III) (m.p. 145–146°; lit.[6] 148°; 0·34%), and

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[3] Bose, P. K., and Finlayson, H. H., *J. Indian chem. Soc.*, 1938, **15**, 516.

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[5] Iriante, J., Kincl, F. A., Rosenkranz, G., and Sondheimer, F., *J. chem. Soc.*, 1956, 4170.

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seselin (IV) (m.p. 120–121°; lit.[7] 119–120°; 0·20%). The percentage of each coumarin based on the weight of air-dried milled plant material is shown in parentheses.

Furanocoumarins are known[8,9] to cause blistering of exposed skin, by the process of photosensitization. Psoralen (I) is the most active, followed by bergapten (II) and xanthotoxin (III). The activity of other furanocoumarins and pyranocoumarins investigated is either slight or absent altogether. The physiological effect of "blister bush" can thus be accounted for by the presence of psoralen (I), bergapten (II), and xanthotoxin (III) in the leaves and branchlets.

Experimental

Air-dried, milled leaves and branchlets of *Phebalium argenteum* (1000 g) were boiled for 2 hr with light petroleum (b.p. 58–60°; 5 l.). The extracted plant was filtered off and air-dried overnight. Batches (200 g each) of the above plant material were extracted for 8 hr in a Soxhlet extractor, with ether (3 l.) previously saturated with water.

The plant residue from the above extractions was allowed to stand at room temperature for one week with methanol (5 l.), and then filtered off and the solvent removed leaving a thick green residue (10 g). The light petroleum and methanol extracts showed only weak fluorescence and were not further investigated.

The combined ether extracts were evaporated to leave a residue (18 g) which could not be effectively partitioned into fluorescent and non-fluorescent fractions using 5% sodium bicarbonate and 5% sodium hydroxide solutions. A sample (1·0 g) of the ether extract residue was dissolved in acetone (10 ml) and applied to two 1-mm thick preparative thin-layer plates of silica gel G (Merck) buffered[10] with 0·3M sodium acetate. The plates were developed in the solvent toluene–ethyl formate–formic acid (5 : 4 : 1 v/v) and visualized under an ultraviolet lamp. The bands were removed individually within the R_F ranges indicated below, and extracted with acetone in a Soxhlet apparatus. The acetone was removed and the constituent of each band identified by nuclear magnetic resonance spectroscopy. The identification was confirmed, after recrystallization of each component to constant melting point, by mixed melting points with authentic samples. The results are summarized as follows:

Band No.	R_F Range	Wt. (mg)	M.P.	Identification
1	0·00–0·07	217	—	aliphatics
2	0·17–0·21	179	—	aliphatics
3	0·24–0·31	189	145–146°	xanthotoxin (III)
4	0·35–0·47	150	189–190°	bergapten (II)
5	0·48–0·61	209	164–165°	psoralen (I)
6	0·61–0·69	112	120–121°	seselin (IV)

There was no evidence of any fluorescent compounds other than those isolated above.

Acknowledgments

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