Preparation and Bioactivity of 1,8-Cineole Derivatives

This thesis is presented for the degree of Doctor of Philosophy at Murdoch University

by

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I declare that this thesis is my own account of my research and contains, as its main content, work that has not been submitted for a degree at any tertiary institution.

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Abstract

The naturally occurring monoterpane 1,3,3-trimethyl-2-oxabicyclo[2.2.2]octane 1, commonly named 1,8-cineole and the major component in the leaf oil of many eucalypts, exhibits bioactivity, being potentially antimicrobial and pesticidal. A range of derivatives of 1,8-cineole and its naturally occurring isomeric analogue 1,4-cineole 2, 1-isopropyl-4-methyl-7-oxabicyclo[2.2.1]heptane, were synthesised. High-cineole eucalyptus oil, 1,8-cineole and the 1,8- and 1,4-cineole derivatives were shown to have a dose dependent pre-emergence and post-emergence herbicidal activity against radish (*Raphanus sativus* var. Long Scarlet), and annual ryegrass (*Lolium rigidum*) in laboratory bioassays. A postulated increase in activity of the ester derivatives due to metabolic cleavage into their bioactive hydroxy-cineole and carboxylic acid portions after uptake by the plant was not observed.

The role of mallee eucalypts in the rehabilitation of degraded farmland in the Western Australian wheat belt, uses of eucalyptus oil and the bioactivity of essential oils and naturally occurring terpenes, with particular emphasis on eucalyptus oil and 1,8-cineole, were reviewed. The review encompasses allelopathic and herbicidal activity, insecticidal, acaricidal and antimicrobial activity.
1,8-Cineole compounds functionalised at position 3 of the cyclohexane ring and the 1,4-
cineole derivatives were chemically synthesised whilst 2-endo-hydroxy-1,8-cineole was
obtained as the primary metabolite of a novel bacterium grown on 1,8-cineole as sole
carbon source. The bacteria were isolated by inoculating liquid growth medium
containing 1,8-cineole as carbon source with aliquots of deionised water in which
eucalyptus leaves had been stirred. Sequencing of its 16S rRNA gene identified the
bacteria as belonging to the order Sphingomonadales, family Sphingomonadaceae and
genus Sphingomonas. Growth curves for the bacterium are described and a metabolic
pathway for the microbial degradation of 1,8-cineole is confirmed. Bacteria were
cultured on a 20 L scale to provide sufficient 2-endo-hydroxy-1,8-cineole for the
herbicidal bioassays.
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