# CHEMICAL INVESTIGATION OF *MYRISTICA CEYLANICA* AND *XYLOPIA NIGRICANS* AND SYNTHETIC STUDIES ON (2*S*,3*R*,1'*R*)-STEGOBINONE

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# CHEMICAL INVESTIGATION OF *MYRISTICA CEYLANICA* AND *XYLOPIA NIGRICANS* AND SYNTHETIC STUDIES ON (2*S*,3*R*,1'*R*)-STEGOBINONE

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## ABSTRACT

This thesis comprises three parts, Part **I**, Part **II** and Part **III**. Part **I** describes the isolation of compounds from the root bark, seed mace/aril and seeds of *Myristica ceylanica* (A.Dc) belonging to family Myristicaceae. All the isolated compounds were tested for mosquito larvicidal assay against the second instar larvae of *Aedes aegypti*. The hexane extract of the root bark yielded 1-(2,6-dihydroxyphenyl)tetradecan-1-one (**81**), malabaricone A (**83**), (7*S*,7'*R*,8*R*,8'*R*)-3,4:3',4'-bis(methylenedioxy)-7,7'-epoxylignane (**92**), (10*Z*,13*Z*)-17-(5-ethyl-6-methylheptan-2-yl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl nonadeca-10,13-dienoate (**148**), $\beta$-sitosterol (**149**) and 4'-hydroxy-3,4-methylene-dioxy-4'-methoxylignane (**150**). The dichloromethane extract of the root bark gave malabaricone B (**41**), 1-(2-hydroxy-6-methoxyphenyl)-9-(4-hydroxyphenyl)nonan-1-one (**86**), (8*R*,8'*R*)-3,4:3',4'-bis(methyledioxy)lignane (**90**) and (7*S*,7'*R*,8*R*,8'*R*)-4,4'-dihydroxy-3,3'-di-methoxy-7,7'-epoxylignane (**94**). Malabaricone C (**42**) was isolated from the methanol extract of the root bark.

The hexane extract of the mace/aril yielded glycerol-2-hexadecanoate-1,3-di(*cis*-9-octadecanoate) (**151**). Its dichloromethane extract gave malabaricone D (**84**). The methanol extract of the mace/aril yielded giganteone A (**106**) and 1-(2,6-dihydroxyphenyl)-4-hydroxy-9-(3,4-dihydroxyphenyl)nonan-1-one (**156**).

The hexane extract of the seeds yielded oleic acid (**153**).

Two esters (**148**) and (**151**) and the diarylalkanone (**156**) were found to be new and their structure elucidations have been described in detail. The lignanes (**90**), (**92**) and (**150**), oleic acid (**153**) and giganteone A (**106**) are isolated from *M. ceylanica* for the first time although lignanes (**90**) and (**92**) have been previously reported from *M. dactyloides* and the other compounds **150, 106** and **153** have been respectively isolated from *Virola calophylla* (Myristicaceae), *M. gigantea* and *Annona muricata* (Annonaceae). Structures were determined by spectroscopic analysis and chemical correlations. The lignanes (**90**) and (**92**) and the arylalkanones (**81**) and (**84**) showed moderate activity against second instar *A. aegypti* larvae.

Part **II** deals with chemical studies on the stem bark of *Xylopia nigricans* Hook f. & Thoms. (Annonaceae). There has been no previous work on this plant. The oxoaporphine alkaloid, 10-methoxyliriodene (**176**) was isolated from its dichloromethane extract together with two kauranes, kauranoic acid (**231**) and 15$\beta$-hydroxykaur-16-en-19-oic acid (**232**). Its methanol extract yielded the oxoaporphine alkaloid, oxoxylopine (**166**) and the isoquinoline alkaloid, (+)-*S*-reticulin (**208**). The kaurane (**231**) showed moderate activity against the second instar larvae *A. aegypti*.

Part **III** of this thesis describes the attempted stereoselective synthesis of stegobinone, (2*S*,3*R*,1'*R*)-2,3-dihydro-2,3,5-trimethyl-6-(1'-methyl-2'-oxobutyl)-4H-pyran-4-one (**271**) the sex pheromone of the drugstore beetle, *Stegobium paniceum*. A synthetic route involving enantiomerically pure (4*R*,5*S*)-5-hydroxy-4-methylhexan -3-one (**282**) and (2*S*,3*S*)-3-tert-butyldimethylsilyloxy-2-methylpentanoic acid (**283**) as building blocks was proposed from retrosynthetic analysis. In an attempt to improve on a previous synthesis, a new route to the hydroxyketone (**282**) was attempted. A mixture of diastereoisomeric forms (**282**) and (**285**) of the hydroxyketone (69% yield) was prepared by treating pentan-3-one with a chiral borontriflate and purified using the lipase catalysed acylation method to give hydroxyketone (**282**) (68% yield, e.e >99%). (1S,2R)-norephidrine (**290**) was converted in two steps to (4R,5S)-3-propanoyl-4-methyl-5-phenyl-2-oxazolidinone (**292**) in an overall yield of 80% as part of the planned synthesis of the acid (**283**), which could not be completed due to time constraints. The synthesisof stegobinone could also therefore not be completed.