REVIEW

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Natural sesquiterpenoids

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This review covers the isolation, structural determination, synthesis and chemical and microbiological transformations of natural sesquiterpenoids. The literature from January to December 2003 is reviewed, and 389 references are cited.

Braulio M. Fraga was born in Tenerife (1944) and received his PhD in Chemistry at the University of La Laguna (1970), where he lectured in Organic Chemistry for several years. In 1971 he was honoured with the Young Researcher Award of the Spanish Royal Society of Chemistry. He obtained a permanent position in the Spanish Council for Scientific Research as Tenured Scientist in 1972, being later appointed Research Scientist (1986) and Research Professor (1987). He was director of the Institute of Natural Products (Tenerife) from 1988–1991, and has been the representative of the Spanish Council for Scientific Research in the Canary Islands since 1991. He had previously been appointed Professor of Organic Chemistry at the University of Valencia (1981). His research interests range from the chemistry to the biotransformation of natural products, especially in the field of terpenes. He has authored more than 190 scientific publications.

Braulio M. Fraga

1 Introduction

The structure and mechanism of action of the enzyme isopentenyl pyrophosphate-dimethylallylpyrophosphate isomerase have been determined.[1] A review of the analytical techniques used in the study of sesquiterpenes and sesquiterpene lactones has appeared.[2] Mutagenesis studies to deduce the structure–function relationships of sesquiterpene synthases and oxidosqualene cyclases have been reviewed.[3] The volatile components of 25 taxa of the liverwort family Frullaniaceae have been analyzed by GC-MS. Two of the chemotypes are characterized by the presence of sesquiterpene lactones and sesquiterpene lactones-bibenzyls.[4] The terpenoid coumarins of the genus *Ferula* have been reviewed.[5] It has been shown that new atmospheric aerosol particles observed in different areas are not caused by monoterpenic products, but are most likely initiated by very volatile substances formed in the reaction of sesquiterpenic hydrocarbons with ozone.[6]

2 Farnesane

The new sesquiterpenes **1–4** and the known (*E*)-β-farnesene have been identified as components of the paracloacal gland secretions of the alligatorids *Alligator sinensis*, *Paleosuchus palpebrosus* and *Paleosuchus trigonatus*. The structure of **1** was confirmed by chemical synthesis and gas chromatography on a chiral phase.[7] Enantiopure (*S*)-2,3-dihydrofarnesoic acid has been identified, for the first time in nature, as a component of the cephalic glands of the male European bee wolf wasp *Philanthus triangulum*.[8] Acetylene sesquiterpenoid esters, **5** and **6**, derived from caulerpenyne have been isolated from the green alga *Caulerpa prolifera*. In these compounds the terminal vinyl acetoxy group of caulerpenyne has been substituted by various fatty acid residues.[9] On the other hand, an efficient synthesis of the bioactive sesquiterpene (±)-dihydrorhipocephalin **7** has been carried out.[10] This tetrahydro analogue of caulerpenyne

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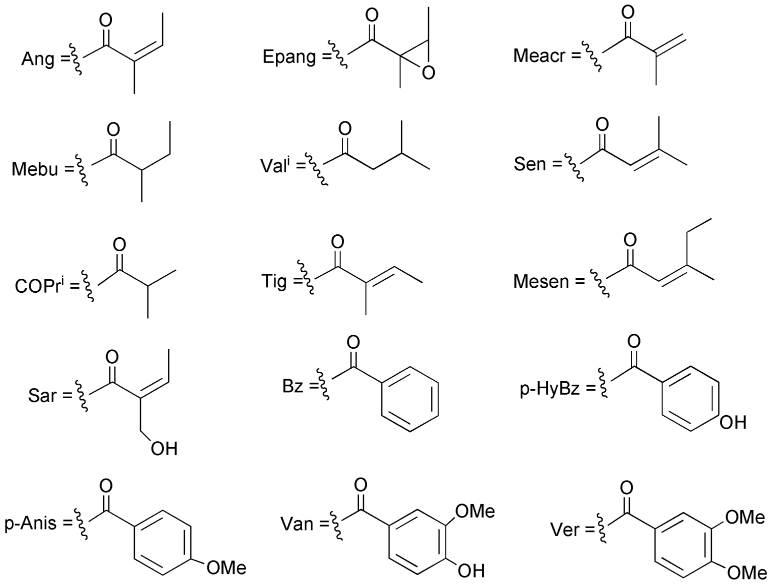
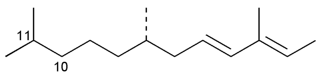
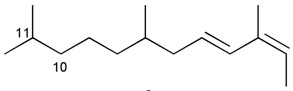


Fig. 1 Structural abbreviations used in this review.

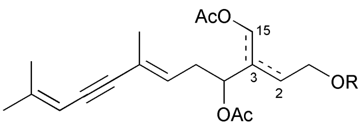
had been isolated from marine algae of the genera *Penicillus* and *Udoteca*. The sesquiterpene (6*E*)-5-tigloxy-9-hydroxy-nerolidol **8** has been found in an extract of the flowerheads of *Achillea pannonica*.[11] Two new polyoxygenated farnesylcyclohexenones with moderate cytotoxicity, deacetoxyyanuthone A **9** and its 2,3-hydro derivative **10** have been obtained from a marine isolate of a fungus, *Penicillium* sp.[12] Niaviolide **11** and epoxyniaviolide **12** are two new macrocyclic sesquiterpenes, which have been found in male secretions of the African butterfly *Amauris niavius*.[13] The biosynthetic origin of the dichloroimine group in stylotellanes A and B has been studied in the sponge *Stylotella aurantium*.[14]



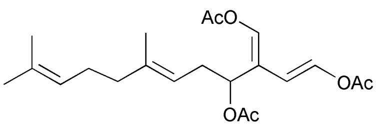
1
2 Δ^{10}



3
4 Δ^{10}



5 R = various $\Delta^{3(15)}$
6 R = various Δ^{2}



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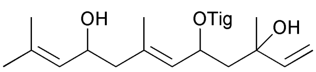

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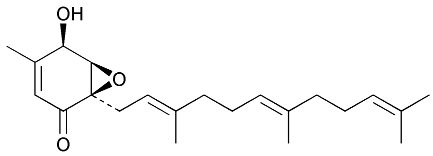

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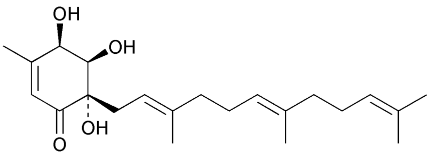

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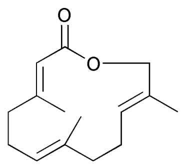

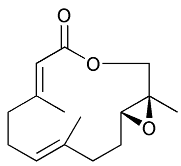

11 **12**

The cloning and sequencing of a gene encoding the farnesyl pyrophosphate synthase of *Trypanosoma brucei* has been reported showing that this enzyme is essential for the viability of this parasite.[15] Three full-length cDNAs encoding putative isoprenoid synthases have been isolated from an *Artemisia tridentata* cDNA library.[16] The roles of α-farnesene in the behaviour of codling moth females, *Cydia pomonella*, have been investigated.[17] When the larvae of the weevil *Oxyops vitiosa* feed on the leaves of *Melaleuca quinquinervia* they produce a shiny orange secretion. Previous studies indicated that one of its components, viridiflorol, is sequestered from the plant and repels fire ants. When the larvae feed on a different chemotype of *M. quinquinervia*, which lacks viridiflorol, (*E*)-nerolidol is sequestered, and a similar protection against the ants with this sesquiterpene is observed.[18] A combination of apigenin and *trans*,*trans*-farnesol inhibits the accumulation and polysaccharide content of *Streptococcus mutans* biofilms without a major impact on the viability of this bacteria.[19] The synthesis and antimicrobial evaluation of farnesyl diphosphate mimetics have been reported.[20]