Natural Products from around the World

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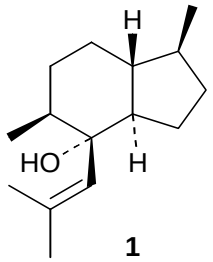
Abstract
In this lecture I want to discuss compounds isolated from a few liverworts, including *Blepharostoma trichophyllum* from Germany and Scottish *Frullania tamarisci.* I shall also talk about the constituents of some Meliaceae, including *Carapa procera* from Guyana and *Swietenia macrophylla* from Barbados. *Garcinia* species are widespread in tropical regions and I shall describe xanthone and benzophenone constituents from some Cameroon, Vietnamese and Indonesian species. Interesting natural products continue to be discovered in Cameroon medicinal plants and I shall discuss, *inter alia,* a terpenoid quinone from *Pycnanthus angolensis.*

Key words : Terpenoids, xanthones, benzophenones, Hepaticae, Meliaceae, *Garcinia* species, *Pycnanthus angolensis*

Two plant families have been of special interest to me throughout my long career in natural products, the Hepaticae (liverworts) and the Meliaceae. I first became interested in the Hepaticae family over thirty years ago. The members of this family, the liverworts, are primitive plants but produce a wide range of terpenoid and aromatic metabolites[1]. Over the years we isolated some unusual sesquiterpenoids including the pacifigorgiane, tamariscol **1**, from *Frullania tamarisci*, gymnomitrol **2** from *Gymnomitrion obtusum*, chiloscypholone **3** from *Chiloscyphus pallescens* and the brasilane, conocephalenol **4**, from *Conocephalum conicum*.



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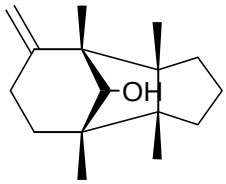

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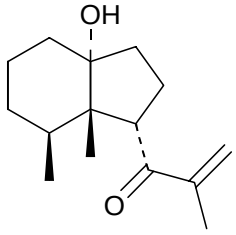

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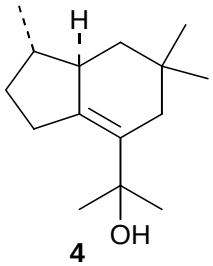

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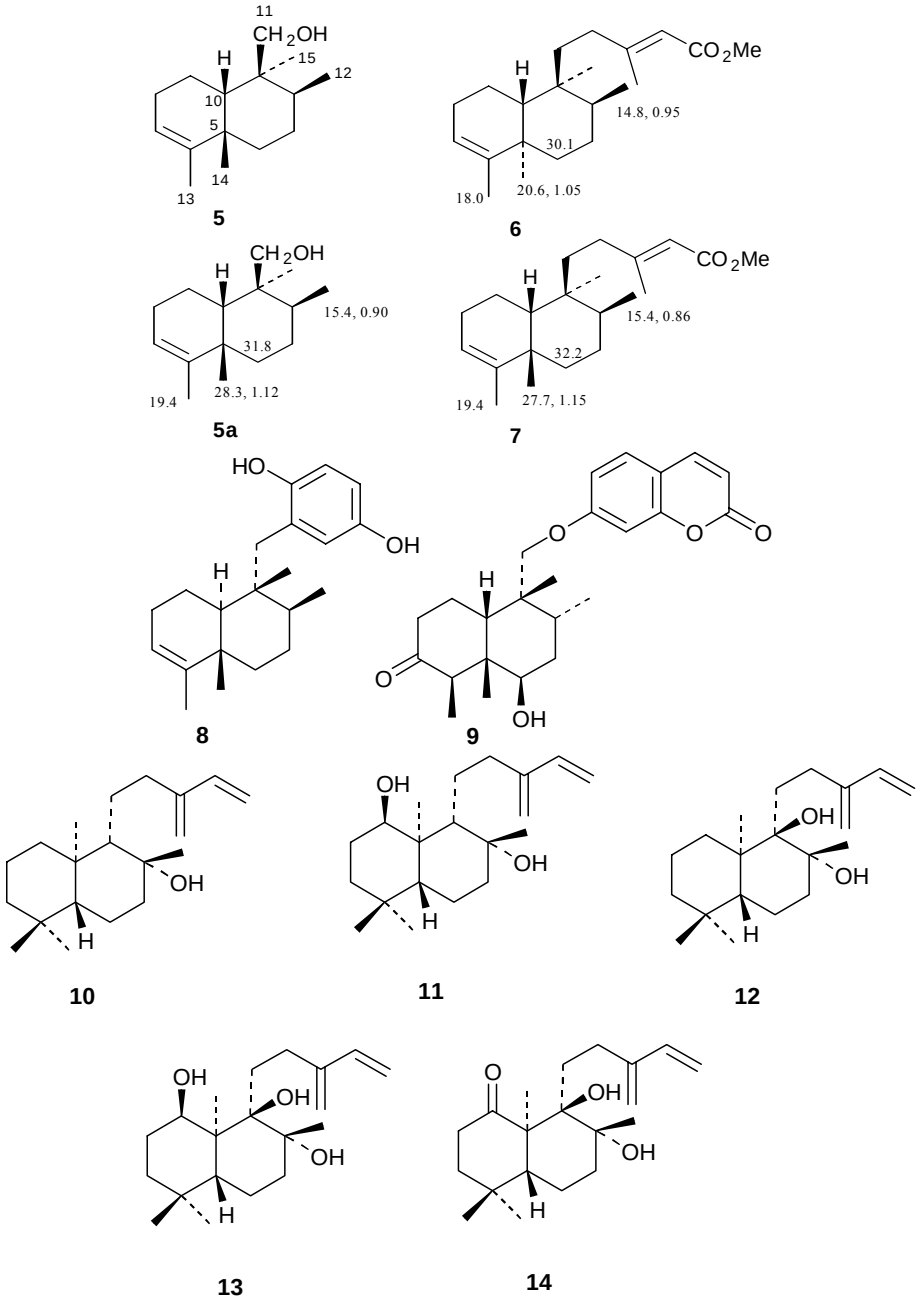
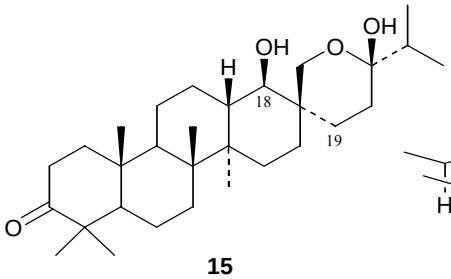
Sometimes liverworts grow in mixture with other species and with mosses. *Blepharostoma trichophyllum* falls into this category and it was difficult to collect sufficient plant material for chemical studies. The problem was solved by growing the liverwort in *in vitro* culture (in the laboratory of Professor H. Becker in Saarbrücken). Extraction and separation (by Dr H.

Feld) afforded a wide range of compounds, including flavone di-*C*-glycosides, bibenzyl derivatives, sesqui- and diterpenoids and hop-22(29)-ene[2]. The most interesting sesquiterpenoid, blepharostol, was shown to have the rearranged drimane structure **5** by the usual spectroscopic methods. NOE difference experiments supported the relative stereochemistry as shown apart from the configuration at C-10. Comparison of selected ^{13}C NMR shifts of blepharostol **5a** with those of the known AB cis and AB *trans* clerodanes **6** and **7** readily revealed that it has an AB cis arrangement. Rearranged drimanes have been reported previously, *e.g.* avarol **8** from the marine sponge *Disidea avara* and kamalol **9** from *Ferula krylovii* but the ring junction stereochemistry is always *trans.* It is possible that blepharostol is a degraded clerodane rather than a drimane derivative. Both drimanes and clerodanes have been reported from liverworts. Other constituents of *B. trichophyllum* include[2] the series of *ent*-labdanes **10-14**.



Triterpenoids are less commonly found in liverworts. However, from an Argentinian liverwort *Lepidozia chordulisera*[3], we unexpectedly isolated the baccharane derivative **15**. The carbon framework was established largely on the basis of correlations of the methyl groups in the HMBC spectrum while the relative stereochemistry and the conformation of rings D and E **16** followed from NOE difference experiments. This compound is closely related to the hosenkosides from *Impatiens balsamina*[4].



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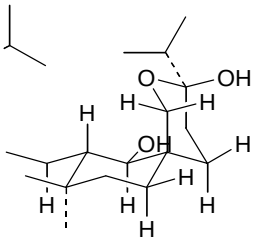

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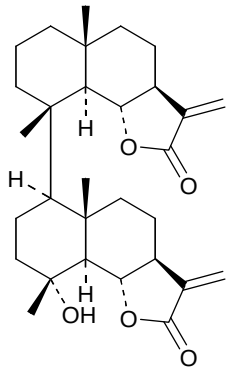
The first liverwort I investigated was *Frullania tamarisci* which grows on the bark of trees and is responsible for dermatitis and allergic reactions among timber workers. The allergenic agents are sesquiterpenoid lactones, *e.g.* frullanolide **17** and the corresponding *trans* lactone γ-cyclocostunolide **18**. In 1987 we isolated a *bis*-eudesmanolide derivative but had insufficient material to establish an unambiguous structure. Recently Professor L.J. Harrison in the National University of Singapore has isolated more of this dimeric compound from Scottish *F. tamarisci* and has established its structure as **19** by X-ray analysis. The compound could be formed as shown by cyclisation of two molecules of costunolide, another constituent of the plant. Related *bis*-lactones have been published by Mues and his colleagues[5].



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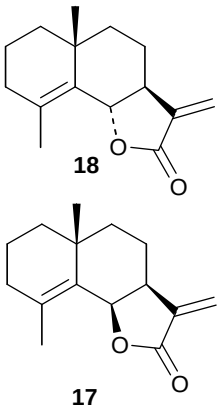
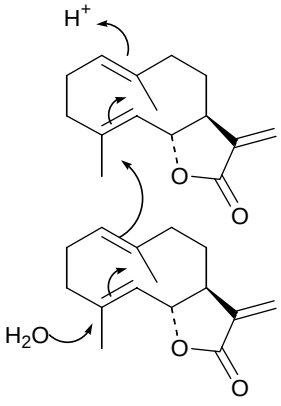
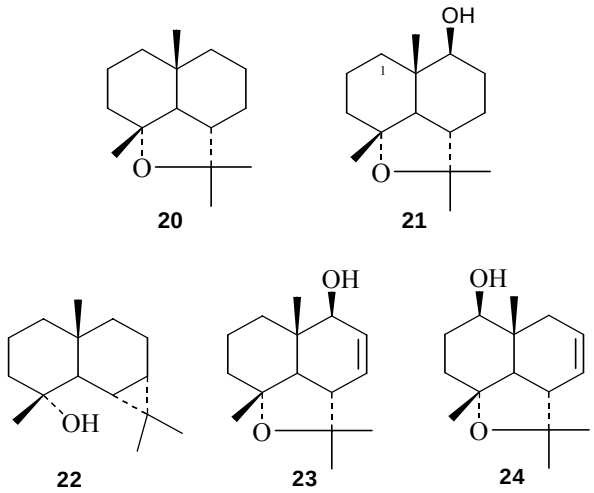


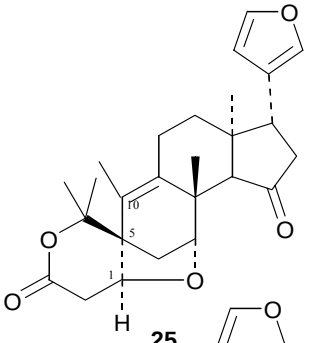
18 **17**



Hashimoto and colleagues have shown[6] that *Aspergillus* species transform the sesquiterpenoid maalioxide **20** into the corresponding 1β- and 7β-hydroxy derivatives. Since we had reasonable amounts of maalioxide and maaliol available from our liverwort investigations Professor Leslie Harrison and Ms. Y Wang in Singapore decided to investigate the effect of a different micro-organism, *Mucor plumbens*, on these substrates. Maalioxide afforded the corresponding 9β-hydroxy-derivative **21** in addition to the previously obtained 1β and 7β alcohols. Under the same conditions maaliol **22** was converted into the unsaturated hydroxy ethers **23** and **24**. Interestingly, these compounds were not obtained directly from maalioxide.



For most of my research career I have been interested in the Meliaceae family. A few years ago we isolated a series of spiro-tetranortriterpenoids, the carapolides **25-28**, from *Carapa procera* and *C. grandiflora*[7]. Carapolide A **26**, a hexanortriterpenoid, was of particular interest since it showed some filaricidal activity. In order to obtain more material for testing we investigated the seeds of *C. procera* from Guyana, in collaboration with Dr. P.-M. Forget (Bruyon, France). The seed extract contains many compounds but separating them from the fats and oils was not trivial. Thus far we have obtained three compounds. The first is the known 7-deacetylgedunin **29**. The other two **30** and **31** are new spiro compounds closely related to the carapolides. The separation was carried out by Dr Hildegard Feld (Saarbrücken) and Dr H. Kamden Wabo (Dschang). The structures and stereochemistry of these compounds were readily established from their HMBC and NOE difference spectra.
Other recent results in this area include the isolation of a simple diene **32**, related to swietenine, from the seeds of *Xylocarpus granatum* (with Professor E. Haque and Dr D.S. Rycroft) and the epoxytiglate derivative **33** from *Swietenia macrophylla* (with Professor W. Tinto and Dr D. Lyder, Barbados). Investigation of the constituents of another Meliaceae species *Turreanthus africanus* (with Professor P. Tane and Dr H. Kamden Wabo, Dschang) resulted in the isolation of three labdanes **34-36** together with a new steroid, 17α,20*S*-dihydroxypregn-4-ene-3,16-dione **37**, whose relative stereochemistry was established by X-ray analysis.



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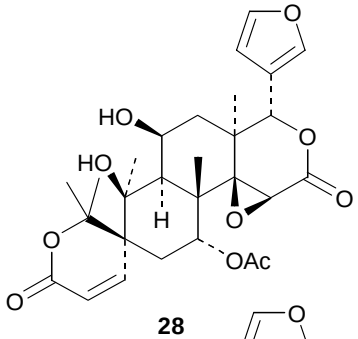

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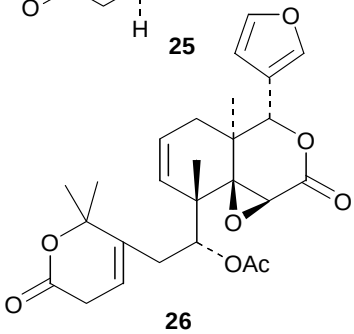

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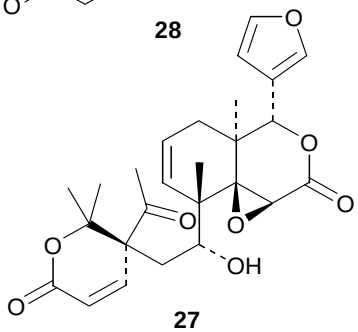

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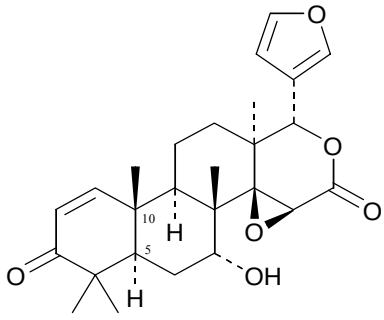

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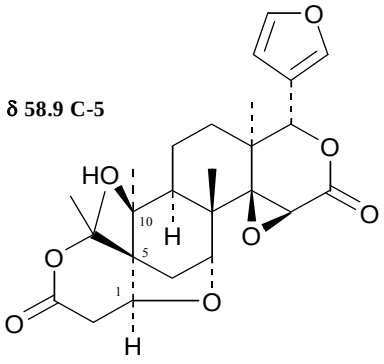
δ 58.9 C-5



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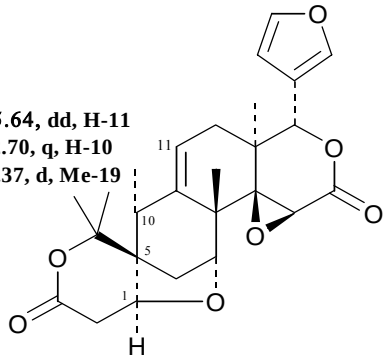
δ 5.64, dd, H-11
2.70, q, H-10
1.37, d, Me-19



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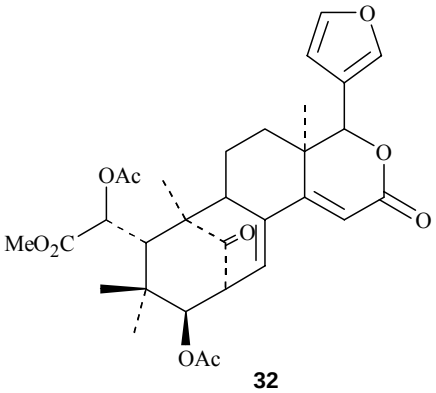

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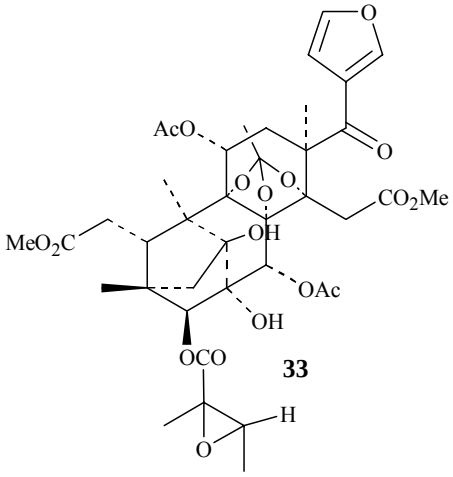

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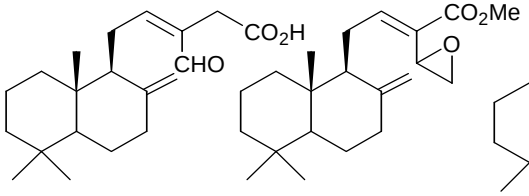
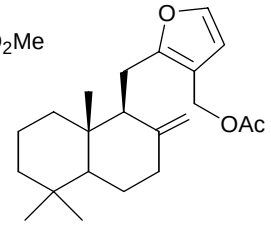


34 **35**



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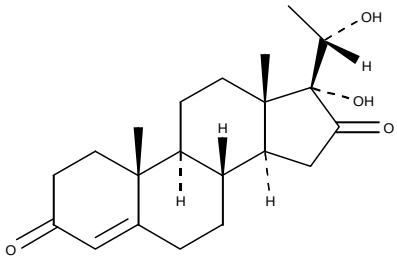

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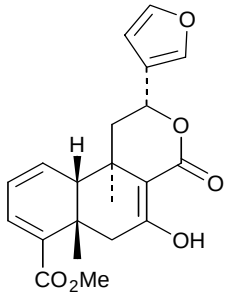
Recently Professor Tane and his colleagues in Dschang isolated a simple *cis*-clerodane, crotomacrine, from *Croton macrostachyus* (Euphorbiaceae)[8]. It has an enolised β-ketolactone system which was revealed by the carbon shifts of C-8 (δ_C 100.5) and C-7 (δ_C 179.1) and the presence of a strongly bonded hydroxyl proton (δ_H 12.78).



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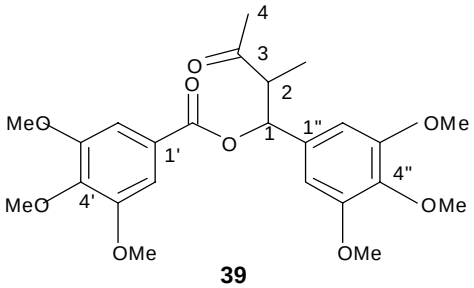
A new cleaved lignan derivative, meiocarpidin **39**, has been found in the stem bark of *Meiocarpidium lepidotum* (Annonaceae)[9]. Its structure followed readily from its proton and

carbon spectra. It is clearly derived from the intact lignan **40** (not known). An example of such a cleaved system has already been reported from *Ocotea foetens*[10] . A new lignan derivative **41** has been isolated from the roots of *Echinops giganteus* where it occurs together with the corresponding hemiacetal[11].



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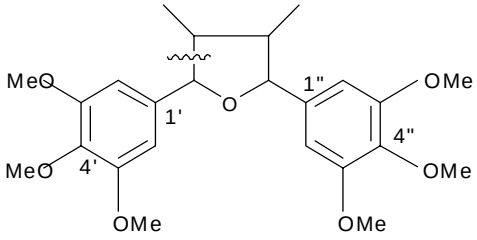

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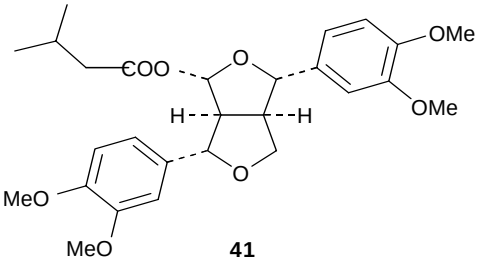

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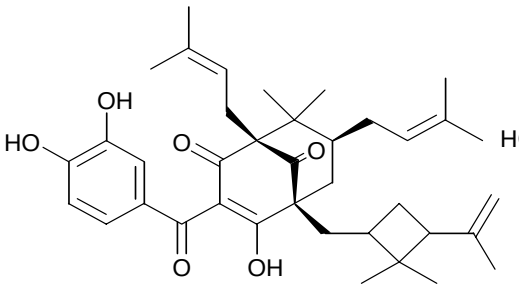
Garcinia species are rich sources of aromatic compounds. From an Indonesian *Garcinia* species the Harrison group in Singapore isolated a new benzophenone derivative **42** which is closely related to garcinol **43** but with an unusual dimethylcyclobutane unit in one of the prenyl side chains. This unit is not very common but has been described before *e.g.* in the sex pheromone component of *Pseudococcus cryptis*[12]. A simpler benzophenone derivative **44** was obtained from the bark of a Vietnamese species, *G. benthami*[13]. Another Vietnamese species, *G. merguensis*, proved to be a rich source of xanthones. Ten compounds were isolated from the bark extract but only one, merguenone **45**, was new[14]. Schomburgxanthones A **47**, B **48** and C **49** are new geranyl xanthones from the bark of *G. schomburgkiana*[15], also collected in Vietnam. These compounds are clearly related to cowanin **46**, a co-metabolite.



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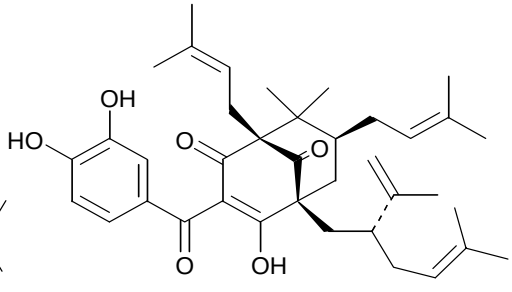

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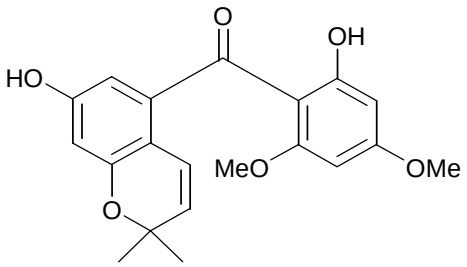

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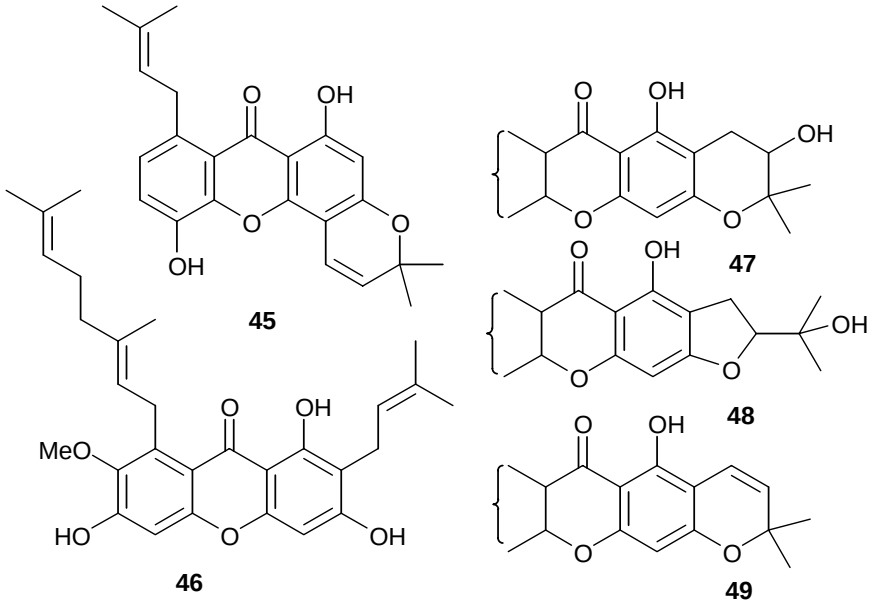
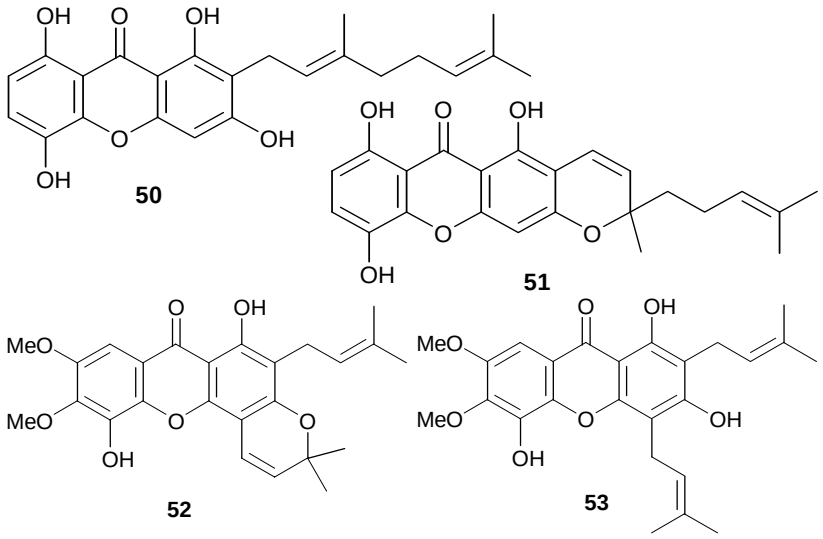
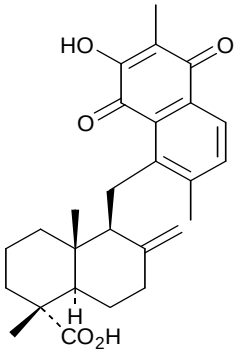


Investigation of the Cameroon species *G. smeathmannii* (with Professor E. Tsamo and his colleagues, Yaoundé) resulted in the isolation of two new xanthones, the geranyl derivative smeathxanthone A **50** and its cyclised congener smeathxanthone B **51**[16]. Two other new xanthones, symphonin **52** and globuliferin **53**, were obtained from the seeds of Cameroonian *Symphonia globulifera*[17,18].



Pycnanthuquinone A **54** is a novel benzoquinone derivative from *Pycnanthus angolensis* (Myristicaceae)[19]. It can be considered as arising by cyclisation of the geranylgeranyl precursor A **55**. The Dschang group has isolated an interesting new benzoquinone **56** from the same plant. It is probable that it also arises by cyclisation of the same type of precursor.



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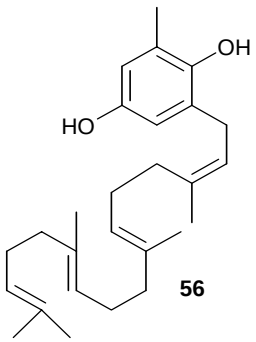

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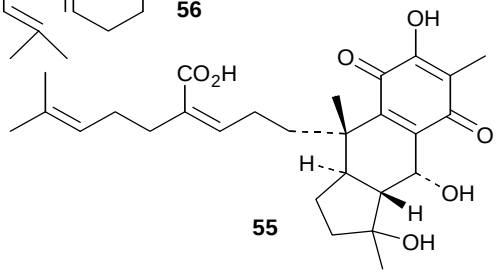

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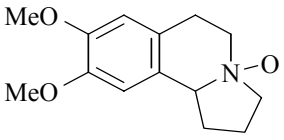
Finally, an investigation of two plants from Mongolia (with Professor Batsuren) resulted in the isolation crispin A *N*-oxide **58**, a new compound, from *Carduus crispus* and arctigenin **59** and matairesinol **60** and their glucosides from *Saussurea salicifolia*.



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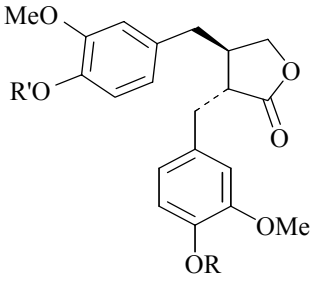

59 R' = OMe; R = H
60 R' = R = H

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