Unusual triterpenoids from African medicinal plants

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Introduction

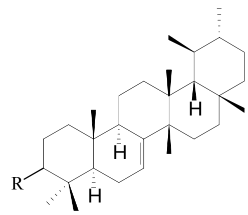
Investigations into the phytochemistry of many African plant species have led to the isolation of many unusual triterpenoids and triterpenoid-derived compounds. Examples of compounds isolated from the Gentianaceae, Rutaceae (Ptaeroxylaceae) and Meliaceae families are discussed.

The Phytochemistry of *Anthocleista grandiflora* (Gentianaceae)

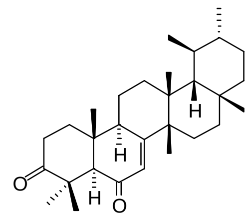
Anthocleista grandiflora Gilg (syn. *A. zambesiaca* Bak.) is a large tree of moist forests in the eastern and southeastern African tropics, and the Comores. *Anthocleista* Afzel. ex R.Br. is a small genus of only fourteen species, eleven of which occur on Continental Africa and three only on the island of Madagascar (Leeuwenberg, 1992). In southern Africa, bark decoctions are used traditionally to treat malaria (Palmer and Pitman, 1972). Regionally, preparations of the bark have also found use as an anthelmintic (specifically for roundworm) (Githens 1949), antidiarrhoeal (Watt and Breyer-Brandwijk 1962; Mabogo 1990), and to treat diabetes, high blood pressure and venereal diseases (Mabogo 1990). Further north on the continent, epilepsy is remedied with the aid of bark decoctions (Neuwinger 2000).

Anthocleista Afzel. ex R.Br. is presently assigned to the Gentianaceae although its affinities were previously considered to be with the Loganiaceae (tribe Potalieae which at times has been recognised as the family Potaliaceae)(Leeuwenberg 1992). Phytochemical (iridoid glycoside presence), morphological and molecular data all support its transfer to the Gentianaceae (Backlund *et al*. 2000). A previous investigation of this species yielded two iridoid glucosides, grandifloroside and methyl grandifloroside, together with the coumarin, scopoletin (Chapelle, 1976). Our re-investigation of the stem bark has yielded four novel triterpenoids, bauerenol, **1**, bauerenone, **2**, 6-ketobauerenone. **3** and grandiflorol, **4**, in addition to scopoletin **5** and (+)-de-*O*-methyllasiodiplodin, **6.** The root bark has yielded, in addition to the above compounds, lupenone, **7 and** the iridoid sweroside, **8**.

The skeleton of grandiflorol, **4**, has not been reported previously and compounds **1-3** are the C-13β-methyl isomer of the bauerane class of triterpenoids. This type of skeleton has been reported once previously in a compound from *Artemisia mongolica* Fisch. ex Bess. (Asteraceae)(Hu *et al*., 2000).



1 R= β-OH
2 R==O



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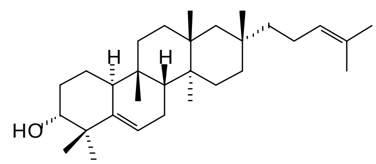

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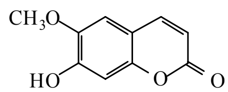

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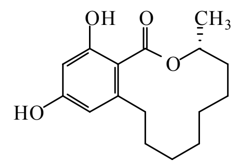

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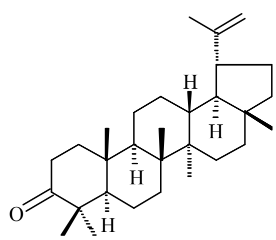

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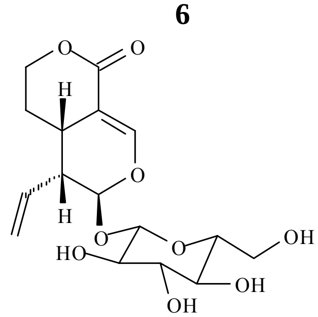

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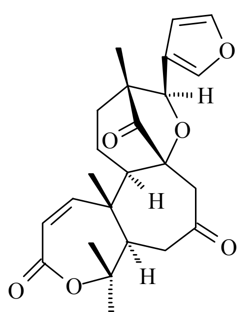
3. The Chemotaxonomy of the Ptaeroxylacaeae

The Ptaeroxylaceae J.Leroy has at various times been placed in the Sapindaceae, Meliaceae, Rutaceae and Simaroubaceae before being widely accepted as a small natural family (Pennington and Styles, 1975; White, 1986). Whereas the family was earlier considered to comprise only two genera (*Cedrelopsis* Baill. and *Ptaeroxylo*n Ecklon & Zeyher, with eight and one species respectively), the monotypic *Bottegoa* Chiov. has more recently been transferred to the Ptaeroxylaceae from the Sapindaceae (Van der Ham et al., 1995). Subsequent *rbc*L sequence analyses (Savolainen et al., 2000) revealed *Ptaeroxylon* to nest within the Rutaceae and to be closely related to the genera *Cneorum* L., *Spathelia* L., *Dictyoloma* A.Juss. and *Harrisonia* R.Br. ex A.Juss. (a genus which had been included in the Simaroubaceae). A number of authors (The Angiosperm Phylogeny Group, 2003) have accordingly referred the Ptaeroxylaceae to the Rutaceae and on the basis of molecular analyses by Chase *et al.* (1999), to a recircumscribed subfamily Spathelioideae. For the purposes of this report we refer largely to taxa of the old Ptaeroxylaceae in relation to Spathelioideae representatives.

Ptaeroxylon obliquum (Thunb.) Radlk., the sneezewood tree, has been found to contain a range of prenylated coumarins and chromones (Dean *et al*., 1966, 1967a, 1967b, 1967c; McCabe *et al*., 1967). Of the eight known *Cedrelopsis* species, all endemic to Malagasy, the chemistry of four has been investigated – *Cedrelopsis gracilis* J.F.Leroy, *C. longibracteata* J.F.Leroy, *C. microfoliata* J.F.Leroy and *C. grevei* Baill. The bark and wood of *C. grevei* have yielded prenylated coumarins and prenylated chromones (Dean and Robinson, 1971; Koorbanally *et al*., 2003) as well as three limonoid derivatives, cedmiline, **9**, cedashnine, **10**, and cedmilinol, **11,** and a quassinoid, cedphiline, **12** (Mulholland *et al*., 1999; Mulholland, *et al*., 2003a**)**. The fruits have been shown to contain prenylated chalcones and prenylated flavanones (Koorbanally *et al*., 2003).

The stem bark of *C. microfoliata* has yielded prenylated coumarins and prenylated flavanones (Koorbanally *et al*., 2002), and the bark of *C. longibracteata* has yielded prenylated coumarins (Randrianarivelojosia *et al*., 2005). The bark of *C. gracilis* has yielded prenylated chromones and two limonoid derivatives cedkathryn A, **13**, and cedkathryn B (Mulholland *et al*., 2004). The limonoid derivatives isolated from *Cedrelopsis* are highly modified, and similar to those isolated from the *Cneorum* (Mondon and Epe, 1983) and *Harrisonia* (Khuong-Huu *et al*., 2001).

The presence of simple and prenylated coumarins and chromones in *Ptaeroxylon*, *Cneorum*, *Dictyoloma* and *Spathelia* and the presence of similar simple limonoids, such as obacunone, and highly oxidised limonoids in *Ptaeroxylon*, *Cneorum*, *Spathelia* and *Harrisonia* further supports the inclusion of these taxa within a recircumscribed Spathelioideae (Rutaceae) rather than the maintenance of a distinct family Ptaeroxylaceae or the placement of *Harrisonia* within the Simaroubaceae. However, *Spathelia* and *Dictyoloma* contain quinoline-derived alkaloids which have not been found in *Ptaeroxylon*, *Cneorum* or *Harrisonia.* Additionally, the isolation of a quassinoid from *Cedrelopsis grevei* is puzzling. Quassinoids are typically found in the Simaroubaceae, with which *Harrisonia* was previously grouped. The isolation of further quassinoids or quinoline alkaloids from these related genera would be of great interest.



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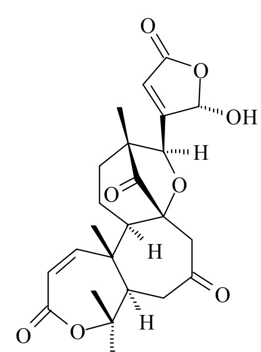

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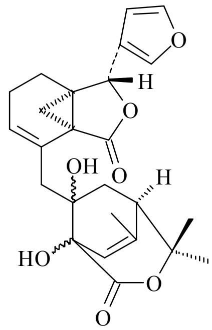

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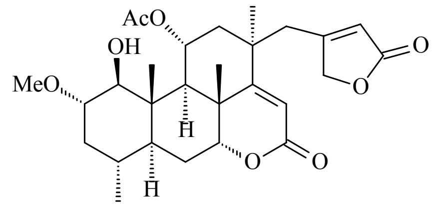

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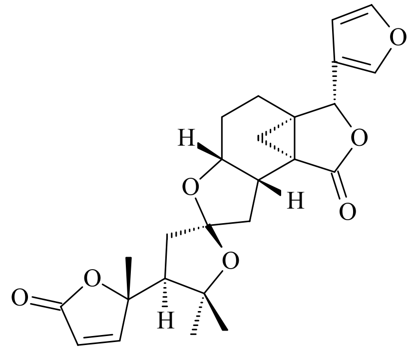

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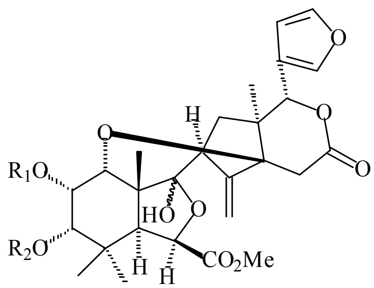
4. Investigations of African Meliaceae species.

The wide variety of possible complex triterpenoid structures can be illustrated by compounds **14-18**, complex tetranortriterpenoids from members of the Meliaceae. Compound **14** has ring B opened to give a C-7 carbomethoxy group and a 8, 30-exocyclic methylene group, a contracted ring C and a ring D which has been oxidised to form a lactone. In compound **15**, additionally, ring A has been expanded into a 7-membered oxygen-containing ring. Both these compounds are derived from the Madagascan species *Astrotrichilia voamata* (Mulholland *et al*., 1999, 2000).



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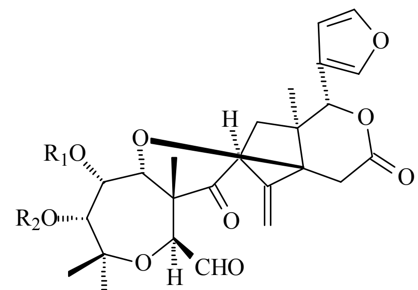

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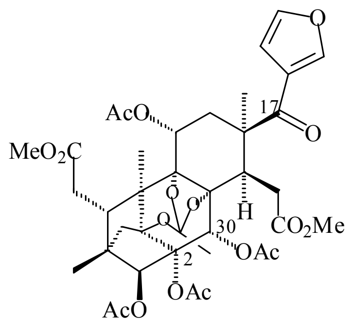
The Malagasy genus *Neobeguea* Leroy has yielded complex limonoids. In leandrianin B, **16**, and C, **17**, from *N. leandriana* J.F.Leroy, ring B gas been opened and recyclised by bond formation between C-2 and C-30 to give phragmalin-type limonoids (Coombes *et al*., 2003). In compounds **16** and **17,** ring D has been oxidised to a lactone, but this is opened to give a keto group at C-17 in compound **18**, isolated from *N. mahafalensis* J.F.Leroy (Mulholland *et al*., 2003b). The presence of a C-1, 8, 9 - orthoester adds to the complexity of these compounds.



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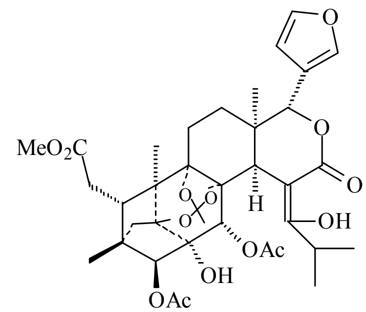

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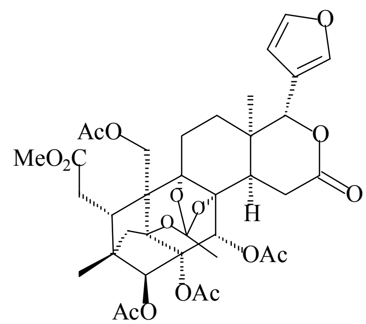

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Conclusion

The large number of possible structures that can be achieved from folding the thirty carbon skeleton in different ways, cyclizations, migrations and other rearrangements, oxidations, ring cleavages and subsequent rearrangements and loss of carbon atoms, leads to an enormous variety of possible structures.

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