The Cyclobuta[b]quinoline alkaloid cyclomegistine from *Teclea gerrardii* I.Verd.
(Toddaliaioideae: Rutaceae)

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Keywords: Rutaceae, Toddaliaioideae, *Teclea gerrardii*, cyclomegistine, quinoline, alkaloids

1. Subject and source

Stem bark from a cultivated specimen of *T. gerrardii* I.Verd. was sourced in Durban, KwaZulu-Natal Province, while fruit was collected at the Lowveld National Botanic Gardens, Nelspruit, Mpumalanga Province, South Africa. Vouchers for the Durban and Nelspruit material (*Crouch 1045*, NH and *Crouch 1110*, NH respectively) have been lodged for verification purposes.

2. Previous work

Acridone and furoquinoline alkaloids have been isolated previously from the stem bark of this species (Kamdem Waffo et al., 2007).

3. Present study

Further investigation of the stem bark of this southern African Rutaceae has resulted in the isolation of the rare cyclobuta[b]quinoline alkaloid cyclomegistine 1 (Fokialakis et al., 2001), while the fruit has yielded the acridone alkaloids melicopicine 2 (Rasoanaivo et al., 1999) and 1,2,3-trimethoxy-N-methylacridone 3 (Ahond et al., 1978; Coppola and Schuster, 1989), and the furoquinoline alkaloid skimmianine 4 (Chakravarty et al., 1999). Structures were established by analysis of their spectroscopic data and comparison with reference values reported in the literature†.

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† Our cyclomegistine 1 was found to be optically inactive, in agreement with that originally reported by Fokialakis et al. (2001), who established the absolute stereochemistry by X-ray crystallography.
4. Chemotaxonomic significance

Although the structures of more than seven hundred and fifty novel acridone and quinoline alkaloids have been published to date (Dictionary of Natural Products, 2008), cyclomegistine 1, from Sarcomelicope megistophylla Hartley (Fokialakis et al., 2001) and S. follicularis Hartley (Chosson et al., 2003), and cyclomegistine B 5, also from S. megistophylla (Mitaku et al., 2007), remain the only reports of metabolites possessing the unusual cyclobuta[b]quinoline skeleton to have appeared in the literature (SciFinder, accessed 22 October 2008). Both taxa were described (Hartley, 1986), subsequent to the revision of Sarcomelicope Engl. (Hartley, 1982), a small rutaceaeous genus of some nine species confined largely to New Caledonia in Australasia.

Cyclomegistine 1 has been shown, by biomimetic synthesis (Fokialakis et al., 2001), to arise from the 1,2,3,4-tetraoxygenated acridone precursor melicopicine 2, which was co-isolated from S. megistophylla and detected by GC-MS in the extract from S. follicularis. Although no melicopicine 2 was isolated in our original (Kamdem Waffo et al., 2007) study on the stem bark of Teclea gerrardii, it has been identified currently from the fruit. This compound had previously been reported from two other members of the genus: the Madagascan T. boiviniana (Baill.) H.Perrier (Vaquette et al., 1974), and, more recently, T. trichocarpa Engl. collected in Kenya (Lwande et al., 1983; Muriithi et al., 2002).

In recent decades Englerian subfamily concepts for the Rutaceae have been largely discredited as unnatural, based on phytochemical (Waterman, 1975; Da Silva et al., 1988) and molecular data (Groppo et al., 2008). Whilst African elements of the Toddalioideae have been well circumscribed chemically (Waterman, 1973; Waterman et al., 1978; Dagne et al., 1988), they have not been dealt with extensively during molecular systematic treatments (e.g. Chase et al., 1999). Even the most recent molecular analysis using two non-coding regions of the chloroplast genome (Groppo et al., 2008) has considered too few African Toddalioideae to provide an unequivocal phylogenetic context for the present chemical findings; Teclea was not sampled, although Sarcomelicope was. However, Groppo et al. (2008) did demonstrate the relatively close relationship of a Melicope-Acronychia clade and a Vepris clade, both of Old World and Oceanian distribution, that should accordingly form part of a newly circumscribed subfamily (possibly a revised concept for the Rutoideae). Da Silva et al. (1988) had earlier approximated this Asian-Australasian-African link in the construction of their Acronychia- and Evodia- tribes, which they noted to be chemically closely allied through, inter alia, the acridones melicopicine 2 and evoxanthine 6. Waterman (1990) subsequently pointed out their deficiencies in not taking cognisance of the generic revisions of Hartley (1974; 1982), who had earlier recognised the close relationships between Acronychia J.R. & G.Forster, Melicope J.R. & G.Forster and Sarcomelicope Engl. Had Da Silva and co-workers been aware of these treatments, they may possibly have modified the circumscription of their Evodia-tribe, in which Melicope was placed.
Notably, molecular studies (Groppo et al., 2008) have recently confirmed the close affinities of these three genera. Groppo et al. (2008) noted that their molecular results provided a framework for revisions of emergent clades within the Rutaceae, and a reinterpretation of the biogeography of the family. The co-incident occurrence of the rare cyclobuta[b]quinoline alkaloid cyclomegisteine 1 and its acridone precursor melicopicine 2 in both Sarcomelicope in Oceania and Teclea Del. in Africa should prompt a re-examination of the phytogeography and/or biosynthetic traits of their particular subfamilial group, one yet to be delineated with formal taxonomic rank. Da Silva et al. (1988) have speculated that radiation of this group (pro parte) has occurred with expansion from southeast Asia westwards into Africa.

Acknowledgements
We thank Mr Bret Parel and Mr. Dilip Jagjivan for GC-EIMS and NMR spectra, respectively, and the University of KwaZulu-Natal and the National Research Foundation (NRF) for financial aid. The KZN Herbarium (SANBI) and Lowveld NBG (SANBI) kindly allowed harvesting of plant material. Members of the staff of the Mary Gunn Library (SANBI) are thanked for facilitating access to literature.

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\text{cyclomegistine 1} \quad \quad \quad \quad \quad \text{melicopicine 2} \quad \quad \quad \quad \quad \text{3}
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\text{skimmianine 4} \quad \quad \quad \quad \quad \text{cyclomegistine B 5} \quad \quad \quad \quad \quad \text{evoxanthine 6}
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