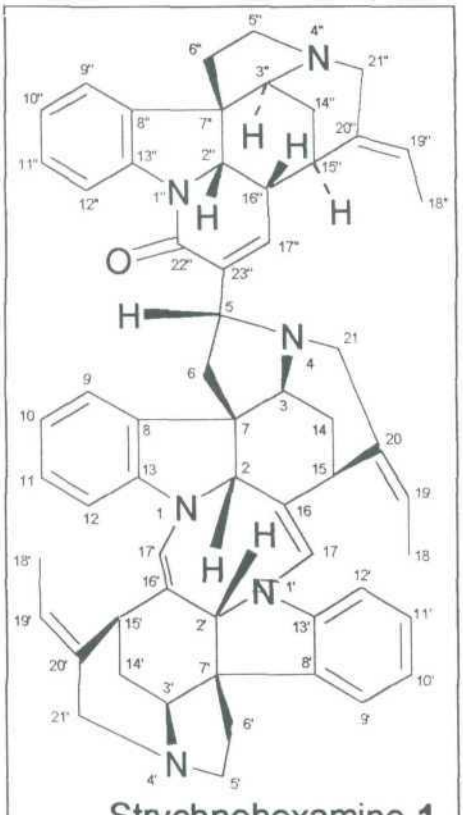
# Strychnohexamine from *Strychnos icaja*, the first naturally occurring indolomonoterpenoid trimeric alkaloid.

Michel Frédérich[a], Geneviève Philippe[a], Elise Prost[b], Jean-Marc Nuzillard[b], Monique Zèches-Hanrot[b], Monique Tits[a], Luc Angenot[a].

[a]*University of Liège, Natural and Synthetic Drug Research Center, Laboratory of Pharmacognosy, B36, Av. de l'Hôpital 1, 4000 Liège, Belgique and* [b]*laboratory of Pharmacognosy, UMR 6013, CPCBAI, BP 1039, 51097 Reims, France.*

*Strychnos icaja* Baill. (Loganiaceae) is a medium sized liana which is found in various vegetation zones of central Africa (rainforest, secondary forest, swamp and gallery forests). *S. icaja* is mainly used as an ordeal poison, but is also occasionally used in traditional medicine, notably for the treatment of chronic and persistent malaria.[1,2] Malaria is the major parasitic infection in many tropical countries, leading to approximately 1.1 millions death each year. In the continuation of our searches for new antimalarial agents, we described the isolation of 6 dimeric asymmetric alkaloids belonging to the strychnan group.[3,4] These alkaloids possess an atypical 5'-23 linkage between the two parts of the substance. This type of linkage is totally original and at this time exclusively described for these alkaloids from *S. icaja*. This kind of liaison could be reproduced in series and could allow the formation of "polymeric" alkaloids.

A reinvestigation of Strychnos icaja roots has resulted in the isolation, from the EtOAC extract, of one tertiary trisindole alkaloid, named strychnohexamine. Its structure has been investigated by means of spectroscopic data interpretation (UV, IR, HRESIMS, 1D and 2D NMR). This is the first time that a natural trimeric indolomonoterpenic alkaloid is isolated directly from a plant species. This compound is one of the largest alkaloids ever discovered.



Strychnohexamine **1**

The alkaloid has been then tested for antiplasmodial activity against *Plasmodium falciparum*, and has been found as moderately active, slightly more than bisnordihydrotoxiferine ($IC_{50}$ in the micromolar range).

References:

1. Neuwinger, H. D. *African ethnobotany: Poisons and drugs, chemistry, pharmacology, toxicology*; Chapman & Hall: London, 1996.
2. Iwu, M. *Handbook of African medicinal plants*; CRC Press: Boca Raton, 1993.
3. Frederich, M.; De Pauw-Gillet, M. C.; Llabres, G.; Tits, M.; Hayette, M. P.; Brandt, V.; Penelle, J.; De Mol, P.; Angenot, L. *Planta Med.* **2000**, *66*, 262-269.
4. Frederich, M.; De Pauw-Gillet, M. C.; Prosperi, C.; Tits, M.; Brandt, V.; Penelle, J.; Hayette, M.; De Mol, P.; Angenot, L. *J. Nat.Prod.* **2001**, *64*, 12-16.