BIOMIMETIC PARTIAL SYNTHESIS OF SOME INDOLE DERIVATIVES

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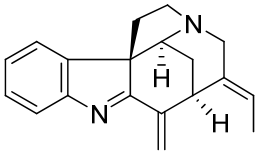
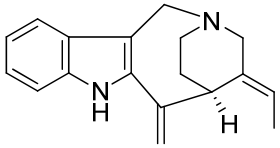
ABSTRACT

Biomimetic partial syntheses of selected indole alkaloids isolated from *Kopsia arborea* were investigated.

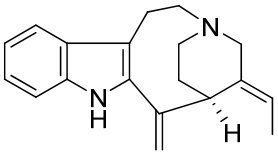
A biomimetic partial synthesis of the new cytotoxic alkaloid, valparicine (**28**) and the 5-*nor*-indole alkaloid, apparicine (**29**) was carried out from pericine *N*-oxide (**43**) (obtained in turn via *m*-CPBA oxidation of pericine **31**) via the Potier-Polonovski reaction. Optimum reaction yields (**28** 10%; **29** 26%) were achieved by carrying out the reaction at 10 ^{o}C, with 4 equivalent excess of TFAA added dropwise, and at high dilution (100 ml CH_2Cl_2), for 10 min. The biogenetic implications of this transformation are discussed. Valparicine (**28**) showed strong cytotoxicity towards human KB and Jurkat cells.



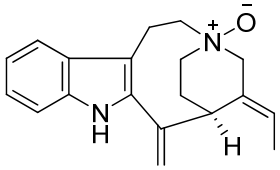
28 Valparicine



29 Apparicine



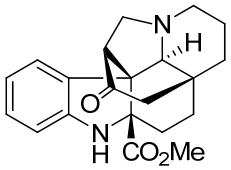
31 Pericine



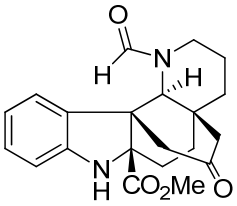
43 Pericine *N*-oxide

A biomimetic electrochemically-mediated semisynthesis of the new ring-opened alkaloid, danuphylline B (**30**), has been achieved via anodic oxidation of the N(1)-Boc-protected methyl chanofruticosinate derivative **51**. Direct electrooxidation of the methyl

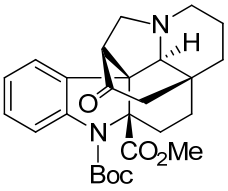
chanofruticosinate precursor **25** did not lead to the formation of any significant product. Installation of the Boc protecting group on the methyl chanofruticosinate precursor **25** gave the N(1)-Boc derivative **51**, as well as the doubly acylated enol carbonate **52**, which was transformed to **51** via Krapcho decarboxylation. Electrooxidation of the N(1)-Boc-protected methyl chanofruticosinate **51** gave the desired iminium salt, which on SiO_2 workup, followed by removal of the Boc group, gave danuphylline B (**30**).



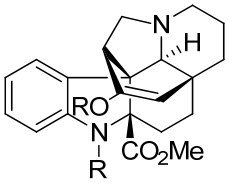
25 Methyl *N*(1)-decarbomethoxy chanofruticosinate



30 Danuphylline B



51



52 R = Boc

ABSTRAK
(BAHASA MALAYSIA VERSION)

Sintesis separa biomimetik untuk alkaloid indola terpilih yang diperolehi daripada *Kopsia arborea* telah disiasat.

Sintesis separa biomimetik untuk alkaloid baru yang sitotoksik, valparicine (**28**) dan alkaloid 5-*nor*-indola, apparicine (**29**) telah dijalankan daripada pericine *N*-oxide (**43**) (yang diperolehi secara pengoksidaan oleh *m*-CPBA pada pericine **31**) secara tindakbalas Potier-Polonovski. Hasil tindakbalas yang optima (**28** 10%; **29** 26%) telah dicapai dengan menjalankan tindak balas pada suhu 10 ^{o}C, 4 kesetaraan berlebihan TFAA ditambah secara titisan, dan pada tahap pencairan yang tinggi (100 mL CH_2Cl_2), selama 10 minit. Implikasi biogenetik untuk transformasi ini telah dibincang. Valparicine (**28**) menunjukkan kesan sitotoksik yang kuat terhadap sel manusia KB dan Jurkat.

Sintesis separa biomimetik elektrokimia terhadap alkaloid gelang-terbuka yang baru, danuphylline B (**30**) berjaya dilaksanakan secara pengoksidaan anodik pada terbitan N(1)-Boc-terlindung methyl chanofruticosinate **51**. Pengoksidaan elektrokimia terus terhadap perintis methyl chanofruticosinate **25** tidak memberikan hasil yang bererti. Pemasangan kumpulan pelindung pada perintis methyl chanofruticosinate **25** memberi derivatasi N(1)-Boc-terlindung **51**, serta enol karbonat yang dua kali diasilkan **52**, yang telah ditukar kepada **51** secara pendekarboksilan Krapcho. Elektrooksidasi N(1)-Boc-terlindung methyl chanofruticosinate **51** memberi garam iminium yang berkenaan, yang mana *workup* dengan SiO_2, diikuti oleh pengeluaran kumpulan Boc memberi danuphylline B (**30**).

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES