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• 中文摘要

利用Cunninghamella bainieri與Aspergillus niger轉換經由isosteviol(ent-16-oxobeyeran-19-oic acid) (1)與m-chloroperbenzoic acid反應所得的 isosteviol lactone (4α-carboxy-13α-hydroxy-13,16-seco-ent-19-norbeyeran-16-oic acid) (2)。受質 2 經由與 C. bainieri 進行微生物轉換得到四個代謝物 3-6，這些代謝物牽涉到 isomerization、hydroxylation 以及環的分裂，接著再進行氧化及選擇性甲基化反應。經由與 Aspergillus niger 進行微生物轉換得到 isomerized、mono-、di-及 trihydroxylated 代謝物 3、4 及 7-12。代謝物 3-12 爲新的化合物，其構造決定是經由 IR、HRFABMS、1D 及 2D NMR；3、4 及 6 的立體組態經由 X-ray 結晶繞射決定。此外，ARE(androgen responsive element)-mediated luciferase reporter assay 被用來篩選 2-6、8-10 及 12 的生物活性，其中 4α-carboxy-15α-hydroxy-15,16-seco-ent-19-norbeyeran-16-oic acid 15,16-lactone (3)、15,16-dioxo-16-methoxy-15,16-seco-ent-beyeran-19-oic acid (6)及4α-carboxy-15α-hydroxy-15,16-seco-ent-1β,7α-dihydroxy-19-norbeyeran-16-oic acid 15,16-lactone (10)表現有意義的結果，特別是 6 的活性表現比參考化合物 testosterone 佳。

• 英文摘要

Two filamentous fungi, Cunninghamella bainieri and Aspergillus niger, were used to investigate the biotransformation of isosteviol lactone (4alpha-carboxy-13alpha-hydroxy-13,16-seco-ent-19-norbeyeran-16-oic acid) (2) which was derived by reacting isosteviol (ent-16-oxobeyeran-19-oic acid) (1) with m-chloroperbenzoic acid. Incubation of 2 with C. bainieri afforded metabolites 3-6 which involved the reactions of isomerization, hydroxylation, and ring cleavage followed by oxidation and selective O-methylation.

Aspergillus niger afforded isomerized, mono-, di-, and trihydroxylated metabolites 3, 4, and 7-12. The structures of metabolites 3-12 were found to be new as deduced by comprehensive analysis using IR, HRMS, and 2D NMR spectroscopic data, with the stereochemistry of 3, 4, and 6 confirmed by X-ray crystallographic studies. Subsequently, 2-6, 8-10, and 12 were assayed as androgen agonists using an ARE (androgen response element)-mediated luciferase reporter gene assay. Among these, 4alpha-carboxy-15alpha-hydr-oxy-15,16-seco-ent-19-norbeyeran-16-oic acid 15,16-lactone (3), 15,16-dioxo-16-methoxy-15,16-seco-ent-beyeran-19-oic acid (6), and 4alpha-carboxy-15alpha-hydroxy-15,16-seco-ent-1beta,7alpha-dihydroxy-19-norbeyeran-16-oic acid 15,16-lactone (10) were found to be significant; in particular, 6 was more active than the reference compound of testosterone.