



## HORSFILINE, AN OXINDOLE ALKALOID FROM *HORSFIELDIA SUPERBA*

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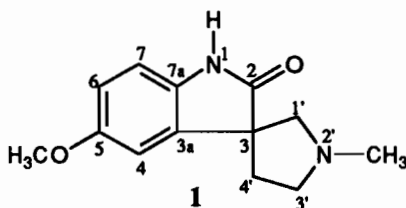
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**Résumé :** un nouvel alcaloïde de type oxindole, l'horsfiline **1**, a été isolé de *Horsfieldia superba* avec la 6-méthoxy-2-méthyl-1, 2, 3, 4-tétrahydro- $\beta$ -carboline **2** et la 5-méthoxy-*N,N*-diméthyltryptamine déjà décrites. La structure de **1** a été déterminée par une analyse spectrale et confirmée par sa synthèse à partir de **2**.

**Abstract :** horsfiline **1**, a new oxindole alkaloid, was isolated from *Horsfieldia superba* together with the known alkaloids 6-methoxy-2-methyl-1, 2, 3, 4-tetrahydro- $\beta$ -carboline **2** and 5-methoxy-*N,N*-dimethyltryptamine. The structure of **1** was determined by spectral analysis and confirmed by partial synthesis from **2**.

### Introduction

Several Myristicaceae are used as sources of intoxicating snuffs, and some of them have been shown to contain hallucinogenic alkaloids, especially those from *Virola* which contain tryptamine derivatives (1). The *Horsfieldia* genus, which encompasses several woody species growing in South East Asia, is sometime used as a medicinal plant (2). Previous phytochemical investigations of the group led to isolation of trimyristin (3), aryl alkanones (4), and lignans (5, 6). Alkaloids were not previously reported in the genus. From *H. superba*, a small tree indigenous to Malaysia, we isolated from the leaves three bases including a new oxindole alkaloid, horsfiline **1** (7).



### Results and Discussion

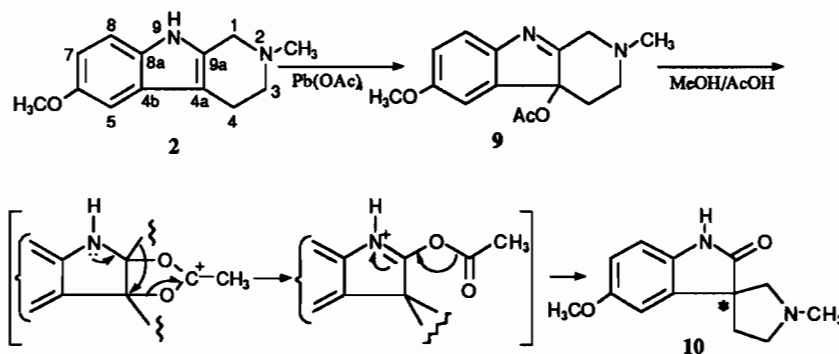
The leaves of *Horsfieldia superba* (Hk. f. et Th.) Warb., were collected at Sandakan (Sabah, Malaysia) in September 1986. Extraction of alkaloids was carried out in the usual way and the three main constituents of the alkaloid fraction were separated by column chromatography and further purified by TLC or crystallization. Two known compounds, 6-methoxy-2-methyl-1, 2, 3, 4-tetrahydro- $\beta$ -carboline **2** and 5-methoxy-*N,N*-dimethyltryptamine **3**, were identified on the basis of their spectral data. Horsfiline **1** was obtained as colorless crystals from acetone, mp 125-126°C, optically active,  $[\alpha]_D^{20} -7.2^\circ$  (MeOH).



The molecular formula  $C_{13}H_{16}N_2O_2$  for horsfiline **1** was determined by HRMS. The structure **1** was proposed from  $^1H$  and  $^{13}C$  NMR data. On methylation with methyl iodide, horsfiline gave a dimethyl ammonium iodide derivative **4**, characterized by spectral measurements.

From a structural point of view, horsfiline appeared to be produced by an oxidative rearrangement of the  $\beta$ -carboline **2** into a 3, 3-disubstituted-2-oxindole. Such a rearrangement have been described especially in the heteroyohimboid and corynantheoid area. A synthesis of horsfiline **1** from **2** was thus attempted.

Oxidation of **2** by N-chlorosuccinimide was first tried. However the preparation of the expected intermediate 4 $\alpha$ -chloroindolenine **5** failed and we isolated further chlorinated and dehydrogenated derivatives: 5-chloro- and 5, 7-dichloro-6-methoxy-2-methyl- $\beta$ -carbolinium chlorides **6** and **7** respectively.



Scheme: synthesis of (±) horsfiline

The reaction of tetrahydro- $\beta$ -carboline **2** with lead tetraacetate, following the Finch *et al.* method, furnished a 4 $\alpha$ -acetoxyindolenine **9** isolated by silica gel chromatography (Scheme). The 4 $\alpha$ -acetoxyindolenine **9** was further converted into the oxindole (±)-horsfiline **10** by an acid catalyzed rearrangement (Scheme I); **10** was obtained as a racemic mixture, mp. 156-157°C. Identity of (-) natural **1** and (±) synthetic **10** horsfilines was deduced from comparison of mass and NMR spectral data.

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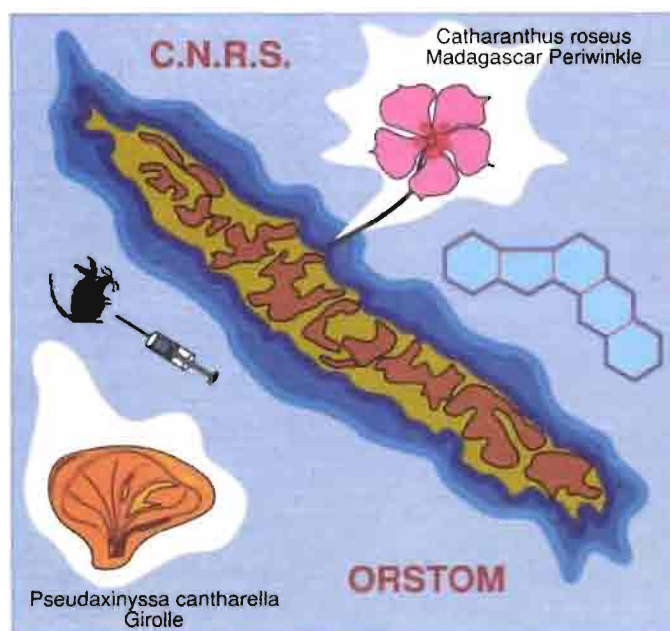
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## ACTES



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