

The Alkaloids of *Machilus duthei*S. FAZAL HUSSAIN,<sup>1</sup> ANJUM AMIN,<sup>2</sup> AND MAURICE SHAMMA*Department of Chemistry, The Pennsylvania State University,  
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(Received 28th September, 1980)

**Summary:** *Machilus duthei* King ex Hook (Lauraceae) has yielded the known aporphines isoboldine (1), boldine (2), laurotetanine (4), and norboldine (5), as well as the N-methyltetrahydrobenzylisoquinoline (+)-reticuline (3).

*Machilus duthei* King ex Hook (Lauraceae) is a large tree growing in the highlands of Azad Kashmir. Since the family Lauraceae is generally rich in isoquinolines, producing such varied alkaloids as benzylisoquinolines, proaporphines, aporphines, oxoaporphines, phenanthrenes and protoberberines,<sup>3</sup> we initiated a study of the alkaloidal content of the roots of this tree. Extraction of 6.5 kg of the dried roots followed by classical acid-base fractionation of the extracts gave rise to 15 g of a crude alkaloidal fraction. This material was further purified by column chromatography on silica gel, followed by thin layer chromatography on silica gel plates. Five alkaloids were thus obtained, each in relatively small quantities considering that 6.5 kg of roots had originally been extracted to furnish 15 g of crude alkaloids. The five alkaloids proved to be isoboldine (1) (1 mg), boldine (2) (6.3 mg), (+)-reticuline (3) (19 mg), laurotetanine (4) (2.3 mg), and norboldine (5) (6.0 mg), all of which were identified by spectral comparisons with authentic samples.

The nmr data for aporphines 1, 2, 4, and 5, at 200 MHz (FT) in deuteriochloroform with tetramethylsilane as internal standard have been summarized in the Table. These aporphines always appear in nature in the dextrorotatory form, so that they all belong to the L-S configuration as indicated in the diagrams.

The benzylisoquinoline reticuline, however, can exist in nature in either the L-(3)-S or the D-(-)-R configuration. Measurement of the circular dichroism curve of the reticuline from *M. duthei* in methanol showed  $\Delta_{\text{enm}}$ : +3.32<sub>285</sub>, -1.39<sub>250</sub>, and +7.30<sub>230</sub>.

The peak at 230 nm is characteristic of N-methylated tetrahydrobenzylisoquinolines belonging to the L-(+)-S configuration,<sup>4</sup> so that our reticuline must be as indicated in expression 3.

It is probable that (+)-reticuline (3) is the biogenic precursor in *M. duthei* for at least some of the four accompanying aporphines.

## Experimental

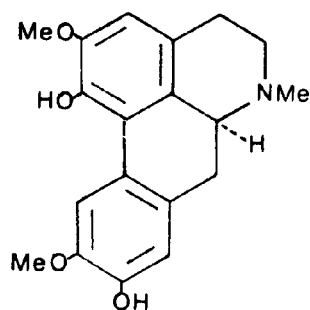
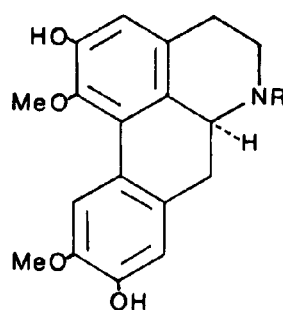
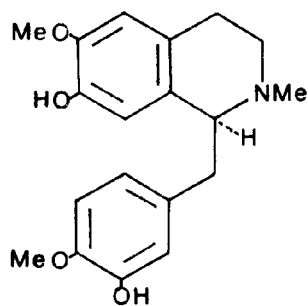
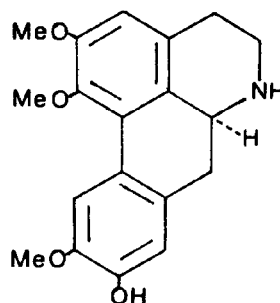
**General Experimental Procedure:** TLC was on Merck silica gel F-254 plates. Spots were visualized under ultraviolet light or by spraying with the chloroplatinate reagent. Due to the small quantities of alkaloids isolated, it was not possible to obtain crystalline samples for melting point determinations.

**Extraction:** The powdered ground roots of *Machilus duthei* (6.5 kg) were extracted with ethanol. Solvent removal gave a semi-solid mass which was taken up in 5% hydrochloric acid, and then filtered. The aqueous layer was extracted with chloroform. Evaporation of the organic layer supplied 36 g of Extract A. The aqueous layer was now basified with ammonium hydroxide to pH 8, and again thoroughly extracted with chloroform. Evaporation of the chloroform furnished 15 g of Extract B. Thin layer chromatography indicated that most of the alkaloids were in this extract.

Extract B was, therefore, passed through a silica gel column, elution being done with chloroform containing increased amounts of methanol. The fractions resulting from elution with 1% methanol in chloroform

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12, R = Me5, R = H34

## NMR Resonances of Aporphines at 200 MHz (FT)

Compound	N-CH <sub>3</sub>	O-CH <sub>3</sub>					
		C-1	C-2	C-10	H-3	H-8	H-11
boldine ( <u>2</u> )	δ2.53	3.60		3.92	6.64	6.84	7.90
Isoboldine ( <u>1</u> )	2.54	—	3.92	3.93	6.55	6.83	8.02
Norboldine ( <u>5</u> )	—	3.62	—	3.91	6.66	6.81	7.92
Laurotetanine ( <u>4</u> )		3.67	3.89	3.92	6.60	6.81	8.09

All the above resonances appeared as singlets. The chemical shifts for the methoxyl groups at C-2 and C-10 in isoboldine, as well as in laurotetanine, are interchangeable.

were devoid of alkaloids.

Elution with higher percentages of methanol in chloroform provided three major fractions labelled B-I to B-III.

*Isoboldine (1) and Boldine (2)*: Successive tic of the alkaloids of group B-I (230 mg), obtained from elution with 2% methanol in chloroform, using first chloroform-methanol (4:1), and then acetone-chloroform-diethylamine (5:4:1) afforded isoboldine (1 mg) and boldine (6.3 mg).

*Reticuline (3), Laurotetanine (4) and Norboldine (5)*: Fractionation of the alkaloids of group B-II (910 mg), obtained by elution with 2% methanol in chloroform, using chloroform-methanol (4:1) and subsequently acetone-chloroform-diethylamine (5:4:1) yield

ded reticuline (19 mg), laurotetanine (2.3 mg), and norboldine (6.0 mg). Group B-III yielded a small additional quantity of norboldine.

#### Acknowledgement:

This research was supported by NIH research grant CA-11450, awarded by the National Cancer Institute, USPHS.

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