

## REVISED STEREOCHEMISTRY FOR THE 4-HYDROXYLATED APORPHINES (+)-GLAUFIDINE AND (+)-EPIGLAUFIDINE

HÉLÈNE GUINAUDEAU<sup>1</sup>

Faculté de Médecine et de Pharmacie, Université de Limoges, 87032 Limoges Cedex, France

and MAURICE SHAMMA

Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802

Fourteen 4-hydroxylated aporphines are presently known (1-3). Four of these, (+)-cataline, (+)-norcataline, (+)-epicataline, and (-)-steporphine, have also been synthesized through selective oxidation at C-4 of their optically active simple aporphine analogs of known absolute configuration (4, 5).

4-Hydroxylated aporphines may belong to either the *R* or the *S* absolute configurations. In this context, they follow the simple rule that applies to all simple, non-C-4-hydroxylated aporphines, namely, that species of the C-6a *R* configuration are levorotatory while the *S* analogs are dextrorotatory (1-3).

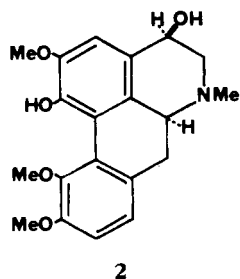
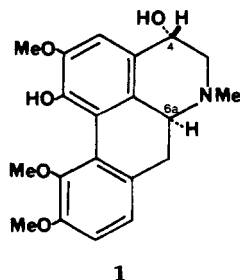
The relative chirality at C-4 was originally derived from <sup>1</sup>H-nmr spectral measurements (4, 6) and was confirmed by an X-ray analysis of *N,O*-diacetyl-4-hydroxynornantenine (7). The generalization that can be drawn is that H-4 appears near  $\delta$  4.50 when *syn* to H-6a, and near  $\delta$  4.90 when in an *anti* relationship. Using the above two simple rules, the stereochemistry for most of the known 4-hydroxylated aporphines has been correctly defined (1-3).<sup>2</sup>

Only a few years ago, however, the 4-hydroxylated aporphine (+)-glaufidine,

$[\alpha]_D + 182^\circ$  (c 0.4, MeOH), was obtained from *Glaucium fimbriigerum* (Papaveraceae) and was assigned structure **1** in which H-4 lies *anti* to H-6a, even though the nmr spectrum shows a broad triplet at  $\delta$  4.46 for H-4. Reduction of (+)-glaufidine resulted in hydrogenolysis of the 4-hydroxyl group and formation of the well-known aporphine (+)-corydine of established *S* absolute configuration (9).

More recently, the diastereomeric alkaloid (+)-epiglaufidine,  $[\alpha]_D + 198^\circ$  (c 0.5, MeOH), was isolated from the same plant source and was given structure **2**, although H-4 was reported to absorb at  $\delta$  4.93 in the nmr spectrum. Again, reduction of (+)-epiglaufidine provided (+)-corydine (10).

Clearly, the stereochemical assignments for (+)-glaufidine and (+)-epi-



<sup>1</sup>Alternate address: CNRS, ERA 317, Centre d'Etudes Pharmaceutiques, 92290 Chatenay-Malabry, France.

<sup>2</sup>The stereochemistry at C-4 for (+)-4-hydroxylbulbocapnine, found in a *Glaucium* species, has never been specified (8). Since in the nmr spectrum H-4 appears at  $\delta$  4.50, H-4 and H-6a must be *syn* to each other. The 4-hydroxyl group is, therefore, above the mean plane of the aporphine nucleus as commonly written, while H-6a is below.

glaufidine should be reversed. H-4 in (+)-glaufidine absorbs at  $\delta$  4.66 and is, therefore, *syn* to H-6a. (+)-Glaufidine is thus represented by expression **2**. Similarly, H-4 in (+)-epiglaufidine appears at  $\delta$  4.93, indicating that H-4 and H-6a are in an *anti* relationship. We conclude that (+)-epiglaufidine is delineated by expression **1**.

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