

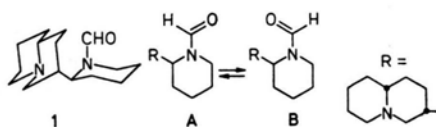
### Rotational Barrier of the Formyl Group in Leontiformine\*

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The hindered rotation about the C–N bond in amides and related compounds is a well-known phenomenon and has been studied by many authors on numerous examples, mainly by the NMR method<sup>1</sup>. A classical example is dimethylformamide, for which the barrier height ( $\Delta G^\ddagger$ ) is 21–22 kcal/mole.

During the process of establishing the structure of the alkaloid leontiformine (**1**) it was found<sup>2</sup> that in the NMR spectrum taken in  $\text{CDCl}_3$  at normal temperature the formyl proton appears as a double signal with equally intensive components located at 1.8 and 1.9  $\tau$ , resp. This effect may be attributed to the existence of two relatively stable (on the NMR time scale) and isoenergetic rotational isomers **A** and **B**:



We found that the doublet structure of the formyl signal of **1** in  $\text{CDCl}_3$  (peak separation  $\Delta\nu = 5.85$  Hz at 60 MHz, 22 °C) remains essentially unchanged up to ca. 60 °C. The spectra taken in dimethylsulfoxide at normal temperature are similar to those in  $\text{CDCl}_3$ , but at higher temperature the formyl signals undergo broadening and finally coalesce at 93 °C; a single sharpening signal is observed above that temperature. The results for **1** and its hydrobromide are presented in the Table, where the values of the rotational barrier  $\Delta G_c^\ddagger$  at the coalescence temperature  $T_c$  were calculated according to the formula<sup>3</sup>:

$$\Delta G_c^\ddagger = 4.58 T_c [9.97 + \log(T_c/\Delta\nu)] \text{ cal/mole.}$$

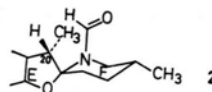
At present, it is generally assumed that the intramolecular factors influencing the rotational barrier in amides are of both electronic and steric origin<sup>1</sup>. The barriers of **1** and **1**. HBr are the same within the error range. This indicates that the basic centre of the molecule (the quinolizidine N) is conformationally

Compound	$\Delta\nu$ [Hz]	$T_c$ [°K]	$\Delta G_c^\ddagger$ [kcal/mole]
Leontiformine ( <b>1</b> )	5.1	366	$19.8 \pm 0.2$
Leontiformine-hydrobromide	5.0	359	$19.5 \pm 0.2$

Table I. NMR-parameters and rotational barriers of leontiformine (**1**) and its hydrobromide in dimethylsulfoxide solution. (Concentrations ca. 0.8 m. Spectrometer JEOL JNM-C-60S (60 MHz).)

remote from the amide bond, unlike the case of the analogous compound<sup>4</sup> containing NH instead of N–CHO. The barrier of leontiformine is close to that of dimethylformamide; the somewhat lower value for **1** should be attributed to the difference in steric rather than in electronic factors.

In order to take into account the influence of the piperidine ring on the barrier, it seems appropriate to compare the value found by us with literature data for other *N*-acylpiperidines. Up to our knowledge, the only *N*-formylpiperidine derivative studied so far is the *O,N*-diformate of 5 $\alpha$ -solasodanol (**2**), which has been resolved chromatographically at normal temperature into two isomers with different chemical shifts of the formyl proton<sup>5</sup>. Although no barrier value has been reported in this case, it is known<sup>6</sup> that such preparative resolution is possible when  $\Delta G_c^\ddagger \geq 23$  kcal/mole. Such a high barrier in **2** could be explained by strong steric interaction of the formyl group with the 20-methyl group in the transition state of the C–N rotation.



Barriers of 15–16 kcal/mole have been measured for some ring-substituted *N*-acylpiperidines<sup>7</sup>. Similar decrease of 3–4 kcal/mole (compared with **1**) on replacement of H by  $\text{CH}_3$  corresponds to the barrier ratio in the pair dimethylformamide-dimethylacetamide<sup>1</sup>.

It is interesting to note the equal population of the rotamers **A** and **B** for **1** and **1**. HBr in  $\text{CDCl}_3$  as well as in dimethylsulfoxide solution. Such phenomenon has been observed also for other cyclic formamides<sup>5, 8, 9</sup>, particularly in nonpolar solvents. On the other hand, for cyclic acetamides and benzamides, a very strong predominance of one rotamer is normally observed<sup>10</sup>.

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