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RE-ASSIGNMENT OF CONFIGURATIONS IN ISOPILOSINE STEREOISOMERS

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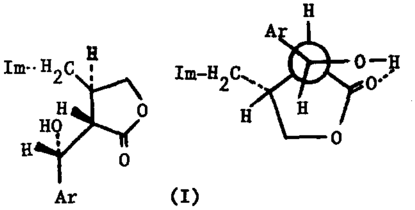
In a recent publication[2] we have described the production of the 6-epimeric isopilosines and assigned their structure on the basis of circular dichroism study. To ascertain the stereochemistry of the above stereoisomers we have undertaken an infrared study of isopilosine and of epiisopilosine and its fluoroderivatives in the hydroxyl (3600-3400 cm^{-1}) and the carbonyl absorption regions of the spectra.

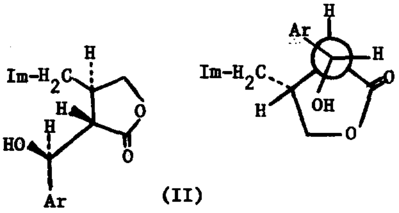
The hydroxyl group in the 6R-epimer is presumably proximate to the lactone carbonyl (I), and its absorption band around 3500 cm^{-1} is expected to be concentration-independent, whereas in the 6S-epimer (II) the case should be just the opposite.

The ir spectrum of isopilosine (1) (mp 182.0-182.5°, $[\alpha]_D^{25}$ + 35.5°) in $CHCl_3$ (0.5%, 0.25%, 0.10%)[3] exhibits a sharp but weak band at 3600 cm^{-1} (free OH) and a broader strong band at 3500 cm^{-1} which does not change on dilution (intramolecular hydrogen-bonding). Similar chloroformic solutions of epiisopilosine (2) (mp 182-184°, $[\alpha]_D^{25}$ - 44.8°) gave notably different ir spectra in which the band at 3605 cm^{-1} is strong while that appearing at 3400 cm^{-1} is weak, broad and concentration-dependent (typical for intermolecular hydrogen-bonding).



(I)

6R-epimer



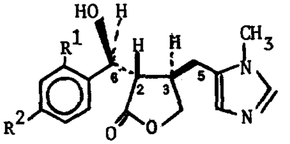
(II)

6S-epimer

Im = 1-methyl-5-imidazolyl

The carbonyl absorption in the former occurs at 1762 cm^{-1} and in the latter at 1769 cm^{-1}.

The pertinent ir data for *p*-fluoroepiisopilosine (3) (mp 165-168°, $[\alpha]_D^{25}$ - 28.2°) (0.1% in $CHCl_3$) are: 3615 (a strong, sharp band), 3390 (weak, broad, concentration-dependent) and 1769 cm^{-1}; and for *o*-fluoroepiisopilosine (4) (mp 207-210°, $[\alpha]_D^{25}$ - 39.9°) (0.07% in $CHCl_3$): 3615 (sharp), 3400 (medium, broad) and 1771 cm^{-1}.

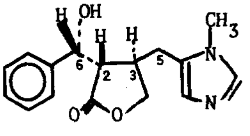


2S, 3R, 6S

(2), $R^1 = R^2 = H$

(3), $R^1 = H$; $R^2 = F$

(4), $R^1 = F$; $R^2 = H$



2S, 3R, 6R

(1)

In contrast to our previous configurational assignments, the data presented here permit the deduction that isopilosine (1) is of the 2S, 3R, 6R configuration whereas epiisopilosine (2), *p*-fluoroepiisopilosine (3) and *o*-fluoroepiisopilosine (4) have the 2S, 3R, 6S configuration,[4] in agreement with the work of Oberhansli cited by Link and Bernauer.[5]

REFERENCES AND NOTES

1. Plantex Ltd., The Dr. O.P. Pfeffer Industrial Center, Natanya, Israel.
2. E. Tedeschi, J. Kamionsky, D. Zeiler, S. Fackler, S. Sarel, V. Usieli and J. Deutsch, J.Org.Chem., 39, 1864 (1974).
3. The ir measurements were taken on a Perkin-Elmer Spectrophotometer, Model 577.
4. For analogous assignment of stereochemistry from ir spectroscopy, see: M. Kuhn and A. von Wartburg, Helv.chim.Acta, 50, 1546 (1967).
5. H. Link and K. Bernauer, Helv.chim.Acta, 55, 1053 (1972).