The Stereochemistry of Illudin S (Lampterol)[1, 2a]

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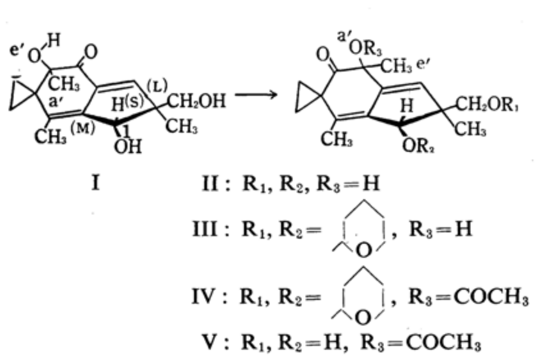
Recently the structure of illudin S,[3] an antitumor substance obtained from a culture liquid of *Clitocybe illudens*, has been proposed. We now wish to propose stereochemical formula I for illudin S on the basis of the following evidence.



The infrared spectrum[4] of illudin S in carbon tetrachloride (7.84×10^{-4} mol.) showed absorption bands at 3631 cm^{-1} (ε, 58.4, free primary OH), 3601 cm^{-1} (ε, 68.4 free secondary allylic OH) and 3485 cm^{-1} (ε, 67.1 bonded tertiary OH), while illudin M,[3] in which the hydroxymethyl group is replaced by a methyl group, showed bands with almost identical intensities at 3601 cm^{-1} (ε, 61.6, free secondary OH) and 3485 cm^{-1} (ε, 71.7, bonded tertiary OH) in carbon tetrachloride (7.72×10^{-4} mol.).

These observations clearly indicate the trans orientation of the hydroxymethyl group and the secondary hydroxyl group.

Isoilludin S[2a, b] (II), formed by the acyloin rearrangement of illudin S with alumina, has infrared absorption bands at 3632 cm^{-1} (ε, 41.4, free primary OH), 3601 cm^{-1} (ε, 56.5, free secondary OH) and 3503 cm^{-1} (ε, 65.2, bonded tertiary OH) in carbon tetrachloride (1.03×10^{-3} mol.). These data show that the tertiary hydroxyl group has a pseudoequatorial conformation in illudin S (the stronger hydrogen bond) and a pseudoaxial conformation in isoilludin S.

The treatment of isoilludin S (II) with dihydropyran and the subsequent acetylation of the dipyranyl compound III, gave IV, which was then hydrolyzed with methanolic hydrogen chloride to monoacetylisoilludin S (V): τ, 8.90, 8.42, 8.31 (methyl groups), 7.89 (2× CH_3CO_2-), 6.58 ($-CH_2OH$), 5.31 (proton α to hydroxyl group), 4.62 (olefinic proton), and 7.95~9.15 (two methylene groups of cyclopropane), whose infrared spectrum in carbon tetrachloride (1.00×10^{-3} mol.) showed, in addition to an absorption band at 3603 cm^{-1} resulting from a secondary hydroxyl group, an absorption band at 2632 cm^{-1} (free primary OH) with a rather decreased intensity and a newly-appeared band at 3532 cm^{-1} (bonded primary OH).

These results provide evidence of the cis orientaion of the hydroxymethyl group and of the tertiary hydroxyl groups in isoilludin S (II).

The stereochemistry of illudin S should, therefore, be represented by formula I in view of the known steric course of acyloin migration.[6]

The absolute configuration of illudin S was determined by applying Horeau's procedure.[7]

When I (0.2×10^{-3} mol.) was treated with (±) α-phenylbutyric anhydride (0.1×10^{-2} mol.),

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[1] Presented at the IUPAC Symposium on the Chemistry of Natural products, Kyoto, Japan, April, 1964.

[2] a) Lampterol, which was isolated from *Lampteromyces Japonicus*, has been proven identical with illudin S on the basis of direct comparison of their nuclear magnetic resonance and infrared spectra as well as mixing melting point.

Cf., H. Shirahama, Y. Fukuoka and T. Matsumoto, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **83**, 1289 (1962); H. Shirahama, Y. Fukuoka and T. Matsumoto, This Bulletin, **35**, 1047 (1962); K. Nakanishi, M. Ohashi, N. Suzuki, M. Tada, Y. Yamada and S. Inagaki, *Yakugaku Zasshi*, **83**, 377 (1963):

b) $C_{15}H_{20}O_4$, m. p. 179~180°C; λ_{max}^{EtoH} 252 mμ (log ε, 4.3) ν_{max}^{KBr} 3420, 1960, 1645, 1365, 1018 cm^{-1}; τ, 8.84, 8.49, 8.32 (three methyl groups), 7.7~8.9 (two methylene groups of cyclopropane), 7.55 (OH), 6.61 (CH_2OH), 5.40 (proton α to hydroxyl group), 4.30 (olefinic proton). Details about the structure of isoilludin S will be reported in the near future.

[3] T. C. McMorris and M. Anchel, *J. Am. Chem. Soc.*, **85**, 831 (1963).

[4] The infrared spectra were measured on a Nippon Bunko grating infrared spectrometer, Model DS-401G, using 50 mm. KRS cell under high resolution condition.

[5] Nuclear magnetic resonance spectra were measured on JNM-3H-60 high resolution NMR spectrometer.

[6] W. A. Jacobs and W. S. Pelletier, *J. Org. Chem.*, **22**, 1428 (1957).

[7] A. Horeau, *Tetrahedron Letters*, 506 (1961); 965 (1962).

the resultant α-phenylbutyric acid showed a rotation of $\alpha_D^{20}+8.75°$ (optical yield, 9.01%). Since the steric requirement of substituents around C_1 can be regarded to be as indicated in formula I, it may be concluded that illudin S should have the absolute configuration of I.

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