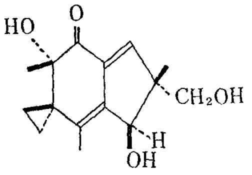
Chem. Pharm. Bull. 12 (7) 856 ~ 857

UDC 615.771.7-011 : 582.238

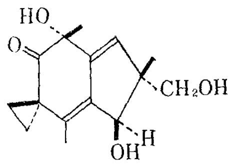
Stereochemistry of Illudin-S (Lampterol)

The relative configurations at the three asymmetric carbon atoms in illudin-S (Ⅰ) and isoilludin-S (Ⅱ)[1] are identical because the former is converted into the latter by an acyloin rearrangement. In the following discussion the absolute configuration of the secondary group is deduced first, and then the configuration at each of the remaining optical centers relative to the secondary hydroxyl is determined.

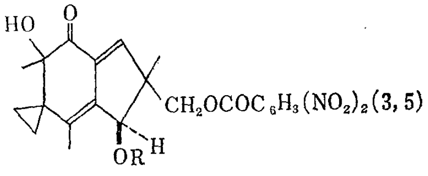
Application of Horeau's asymmetric synthesis[2] to illudin-S mono-3,5-dinitrobenzoate (Ⅲ), m.p. 177~178°, led to an esterification yield of 28% with a neglegible optical yield. This implies that the substituents at the carbinol center have similar steric requirements, and that the so-called "benzoate rule"[3] cannot be employed for interpreting the difference in $[\phi]_D$ values of the monoester (Ⅲ) and diester (Ⅳ), m.p. 167°. However, in situations where the two substituents at a carbinol center have similar steric requirements but differ in polarizability, the rotational shift in going from carbinol to ester can be used to determine the configuration.[3,4] The environment of the secondary hydroxyl in illudin-S clearly presents such a situation, since there is a large difference in the polarizability of the two adjacent carbons, the sp^2 carbon naturally being the more polar. The large positive shift, +623°, in going from the monoester (Ⅲ) to the diester (Ⅳ) permits assignment of the absolute configuration to this optical center as shown.



Ⅰ : illudin-S



Ⅱ : isoilludin-S



Ⅲ : R=H, $[\phi]^{25}_{D}$ −405° (c=0.1419, dioxane)
Ⅳ : R=$COC_6H_3(NO_2)_2$ (3,5), $[\phi]^{25}_{D}$ +217° (c=0.1388, dioxane)

The hydroxymethyl and secondary hydroxyl groups are considered to be in a *trans* relationship since a detailed infrared study of illudin-S in the O-H stretching region does not show any evidence of intramolecular OH···OH bonding. Namely, a 10^{-3} mole solution of illudin-S in carbon tetrachloride had bands at 3636 (free $-CH_2OH$), 3615 (free -CHOH) and 3510 cm^{-1} (C=O···H-O of α-ketol); at higher concentrations (in chloroform solution) the intensity of the two free hydroxyl bands decreased and a broad band at 3500~3300 cm^{-1} (associated OH) appeared.

Molecular models of isoilludin-S show that its six-membered ring can exist in two conformations; in one of them the adjacent *tert*-hydroxyl is *quasi*-equatorial while in the other the methyl is *quasi*-equatorial. The infrared spectrum of isoilludin-S mono-3,5-dinitrobenzoate (primary OH esterified), m.p. 175°, in carbon tetrachloride had a distinct band at 3510 cm^{-1} due to bonding of the *tert*-hydroxyl to the carbonyl. Thus the *tert*-hydroxyl is *quasi*-equatorial. The fact that the same band persisted in the solid state spectra of various monobenzoates of isoilludin-S including the 3,5-dinitrobenzoate and the *p*-iodobenzoate, m.p. 147~148°, implies that the six-membered ring has the

---

[1] M. Tada, Y. Yamada, M. Ohashi, N.S. Bhacca, K. Nakanishi : This Bulletin, **12**, 853 (1964).
[2] A. Horeau : Tetrahedron Letters, **1961**, 506, 654; **1962**, 965.
[3] J.H. Brewster : Tetrahedron, **13**, 106 (1961).
[4] J.A. Mills : J. Chem. Soc., **1952**, 4976.

same conformation in both the dissolved and the solid state and that the *tert*-hydroxyl is *quasi*-equatorial. Since the X-ray studies carried out by Professor Saito and co-workers⁵⁾ on the above mentioned *p*-iodobenzoate show that it is the *quasi*-equatorial group that is *cis* with respect to the *prim*-hydroxyl, it follows that the *tert*-hydroxyl and *prim*-hydroxyl are *cis*-oriented. This leads to the full stereochemistry of illudin-S (lampterol) and isoilludin-S (isolamterol) as shown in formulae (I) and (II), respectively.

The authors are grateful to Professor Y. Saito and Mr. S. Onuma for discussions and disclosure of the X-ray results prior to publication.

Department of Chemistry,
Tohoku University,
Sendai, Japan

Koji Nakanishi (中西香爾)
Masaru Tada (多田 愈)
Yasuji Yamada (山田泰司)

Received June 5, 1964

---

5) Private communication from Professor Y. Saito, University of Tokyo. To be published.