# The Absolute Configuration of Illudin S; Application of the Dibenzoate Chirality Rule

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*Summary* The dibenzoate chirality rule has been extended to the phenol (III) derived from illudin S, and this establishes the absolute configuration of the latter [represented by (I)].

THE planar structure and relative configuration of the anti-tumour antibiotic, illudin S[1] (lampterol[2,3]) which is present in the bioluminescent fungus *Clitocybe illudens* and *Lampteromyces japonicus*,[4] has been established by chemical reactions, spectroscopy, *X*-ray, and more recently by synthesis.[5] However, the absolute configuration remains to be established in spite of several attempts to elucidate it by chemical or spectroscopic methods.[2] The recently developed dibenzoate chirality rule[6] has been extended to the phenolic derivative (III) and this establishes that illudin S possesses the absolute configuration depicted in (I).

Selective esterification of the primary alcoholic function of illudin S (I) with pivaloyl chloride in pyridine and chloroform gave, in good yield, monoester (II); $\nu_{max}$ ($CHCl_3$) 3460, 1722, 1700, 1652, and 1609 cm$^{-1}$, $\lambda_{max}$ (EtOH) 227·0 ($\epsilon$ 9600) and 315·0 nm (2400), $\delta$ ($CDCl_3$) 6·57 (s, olefinic H), 4·69 [s, CH(OH)], 4·07 (m, $CH_2O$, and 2-OH), 1·70 (s, olefinic

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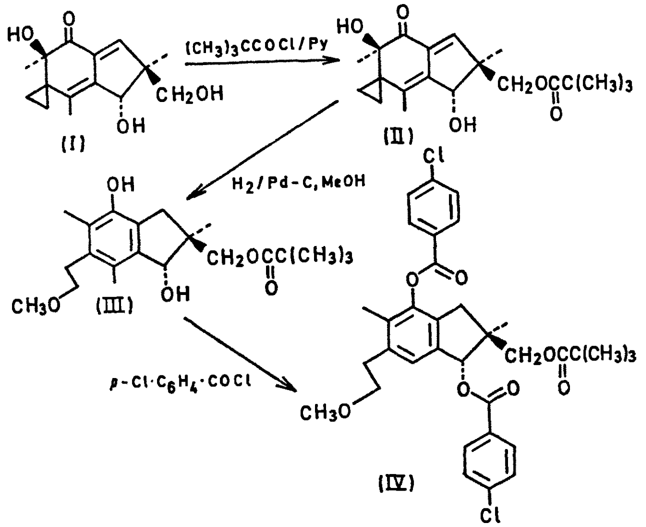
CH$_3$), 1·37 [s, CH$_2$(OH)], 1·23 [s, CH$_3$(CH$_2$O)], 1·13 (s, Bu$^t$), 1·30—0·3 p.p.m. (m, cyclopropane H). Hydrogenolysis of monoester (II) with Pd–C in methanol[1] afforded phenol (III); $\lambda_{max}$ (MeOH) 280·0 inflection, 286·5 nm, $\delta$ (CDCl$_3$) 4·92 [s, CH(OH)], 3·93 (s, CH$_2$O), 3·43 (s, OCH$_3$), 3·5—3·0 (m, OCH$_2$CH$_2$Ph), 2·74 (s, cyclic CH$_2$), 2·36 (s, aromatic CH$_3$), 2·24 (s, aromatic CH$_3$), 1·27 [s, CH$_3$(CH$_2$O)], and 1·14 p.p.m. (s, Bu$^t$). Benzoylation of phenol (III) with *p*-chlorobenzoyl chloride in pyridine at room temperature gave the di-*p*-chlorobenzoate (IV); $\lambda_{max}$ (EtOH) 242·5 nm ($\epsilon$ 35,500), $\delta$(CDCl$_3$) 8·3—7·4 (AB q, aromatic H), 6·61 [s, CH(OCO-)], 4·00 (s, CH$_2$OCO), 3·36 (s, OCH$_3$), 3·4—2·8 (m, OCH$_2$CH$_2$Ph, and cyclic CH$_2$) 2·22 (s, aromatic CH$_3$), 1·26 [s, CH$_3$(CH$_2$O)], and 1·16 p.p.m. (s, Bu$^t$), C$_{35}$H$_{38}$Cl$_2{}^{35}$O$_7$ (*M*$^+$ at *m/e* 640).



The c.d. spectrum of dibenzoate (IV) showed strong Cotton effects, $\Delta\epsilon_{248}$ $-18·2$, $\Delta\epsilon_{229}$ $+12·6$ (in ethanol, Figure 1), the shape, positions and intensities of extrema all being typical for two interacting *p*-chlorobenzoates.[6] The red-shift in the c.d. maxima as compared to ordinary benzoates (233 and 219 nm) is due to the *p*-chloro-substituent.[7] That the c.d. maxima are located at wavelengths similar to those of typical steroid di-*p*-chlorobenzoates (247 and 230 nm)[6] indicates that the nuclear benzene ring is not conjugated to the phenolic *p*-chlorobenzoate chromophore, a fact which can be accounted for by operation of *ortho*-steric effects.

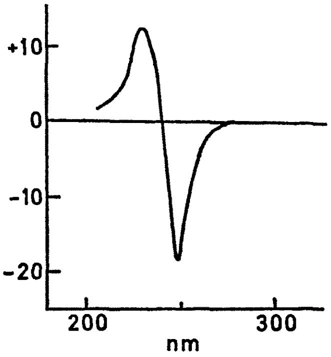


FIGURE 1. *C.d. spectrum of di-*p*-chlorodibenzoate* (IV) *in ethanol.*

The first negative Cotton effect indicates that dibenzoate (IV) has a negative chirality between the 1,4-dibenzoyloxy-groups (Figure 2). The absolute configuration of illudin S therefore should be represented by structure (I).

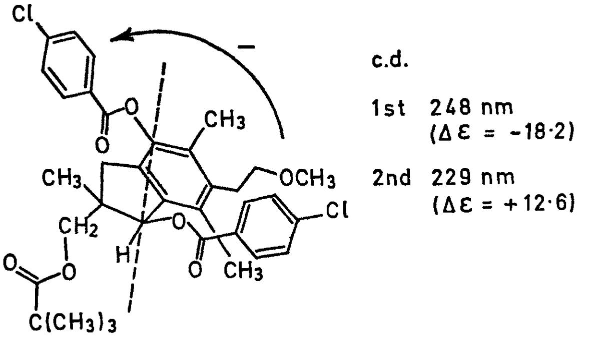


FIGURE 2. *The negative chirality of dibenzoate* (IV).

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