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THE STEREOCHEMISTRY OF C_{15} IN ANNOTININE

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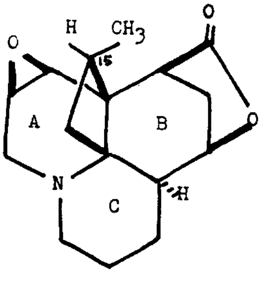
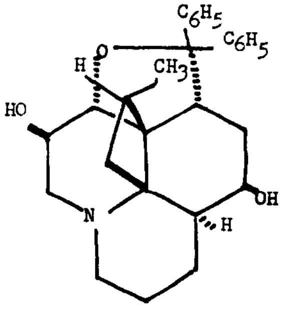
The structure of the Lycopodium alkaloid annotinine (I) and the configuration of all its asymmetric centers except C_{15} was deduced by Wiesner and his coworkers (1), and was later fully corroborated by an X-ray diffraction analysis of the derived bromohydrin (2). Recently, an elegant first total synthesis (3) of annotinine has been announced from the New Brunswick school. However, no evidence concerning the relative stereochemistry of C_{15} has been forthcoming from chemical degradations due to the fact that correlation between this particular asymmetric carbon atom and other functionalities in the molecule is not possible.



I



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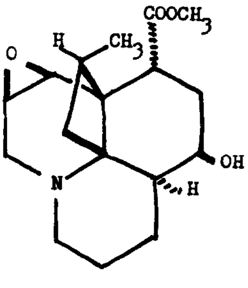

III

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In the present communication we wish to report some results of an n.m.r. study which dramatically confirm the assignment of the configuration of the C-methyl group in annotinine by X-ray crystallography. Diphenylannotinine (II) (4), of known constitution shows an unexpectedly high field three-proton doublet (τ 9.80, J= 6.4 Hz), attributed to the secondary C-methyl group. In annotinine itself the corresponding methyl absorbs at τ 8.74 (d, J= 7.2 Hz) and in methyl epiannotinate (III), the signals appear at τ 8.89 (d, J= 7.0 Hz).

The strong shielding effect imposed on the methyl signals of diphenylannotinine is inevitably the consequence of the magnetic anisotropy of one of the phenyl groups. Formation of an additional tetrahydrofuran ring has rendered the molecule extremely rigid, furthermore, the two benzene rings have to assume a definite conformation in order to minimize nonbonded interactions between themselves as well as with the nearby hydrogen atoms of the parent ring skeleton. Examinations of Dreiding models clearly indicated that the methyl group, only when pointing towards ring B, should experience an enormous shielding by the β-oriented benzene ring.

All the n.m.r. spectra were recorded in deuterated chloroform using TMS as internal standard on a Varian A-60 Spectrometer.

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