The Structure of Fumitremorgin B (FTB), a Tremorgenic Toxin from *Aspergillus fumigatus* Fres

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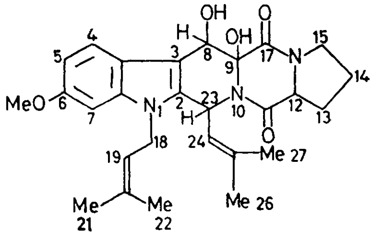
Summary The structure of fumitremorgin B, one of the indole metabolites of *Aspergillus fumigatus* Fres. has been established as (**1**).

Two tremorgenic toxins, fumitremorgin A and B (FTA and FTB) were isolated from a strain of *Aspergillus fumigatus* Fres. found growing on rice.[1] The molecular formulae of these 6-methoxyindole compounds have now been established as $C_{32}H_{41}N_3O_7$ (M^+ m/e 579) and $C_{27}H_{33}N_3O_5$ (M^+ m/e 479) respectively. We now report the structure of FTB, colourless needles (methanol), m.p. 211—212° to be (**1**).

Proline and 6-methoxyindole groups were shown to be present in FTB by n.m.r. spectroscopy; proline was also detected after hydrolysis (6N-HCl) of FTB. The observation of amide bands at 1685 and 1655 cm^{-1} in the i.r.-spectrum of FTB suggested the presence of a dioxopiperazine ring in the molecule[2] formed from two amino-acids, 6-methoxytryptophan and proline.



(1)

The participation of two isoprenyl units in the molecule was clearly demonstrated by the n.m.r. spectrum. A signal at 4·52 p.p.m., (d, 2H) assigned to the methylene adjacent to the nitrogen atom was coupled with the olefinic proton at 5·04 p.p.m., indicating that one of the two isopentenyl groups is located at position 1 of the indole ring. The position of the other isopentyl group was established by a signal at 5·97 p.p.m. (1H, methine N–*C*H) which showed a vicinal coupling with an olefinic proton at 4·76 p.p.m. The reaction between Ehrlich's reagent and FTB was negative, supporting the presence of a substituent at position 2 of the indole ring.

Reduction of FTB with Pd–C gave a dihydro-derivative ($FTBH_2$), $C_{27}H_{35}N_3O_5$ (M^+ *m/e* 481), m.p. 179—180·5°, which showed (n.m.r.), the disappearance of the signals due to the two methyl groups and the olefinic hydrogen atom of the isoprenyl group attached to N(1). When FTB was hydrogenated with PtO_2, a tetrahydro-derivative ($FTBH_4$), $C_{27}H_{37}N_3O_5$, (M^+ m/e 483), m.p. 97—100° was obtained. The n.m.r. spectrum of $FTBH_4$ revealed that both of the isoprenyl groups had been hydrogenated.

N.m.r. and i.r. spectroscopy showed that one hydroxy-group (secondary) is located at position 8 and another (tertiary) at 9.

The base peak appeared at *m/e* 311 ($C_{20}H_{25}NO_2$) owing to the elimination of the dioxopiperazine fragment; this was supported by the appearance of the base peak at *m/e* 313 in the mass spectrum of $FTBH_2$.

A comparison between FTB and lanosulin[3] showed that they were identical although an alternative structure had been proposed.

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