

THE STRUCTURE OF FUMITREMORGIN A

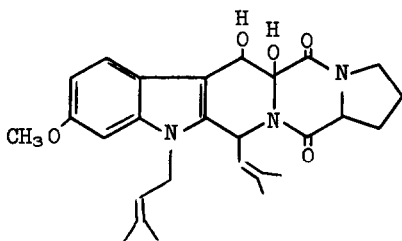
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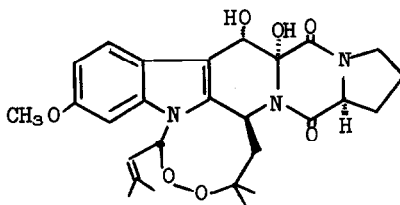
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Recently there has been considerable interest in tremor-producing metabolites from fungi.¹ We¹ and others² have been interested in a class of tremorgens that formally constitute a combination of tryptophan, proline, mevalonate derived units and oxygen. Yamazaki² has reported on the isolation and structure (without stereochemistry) of fumitremorgin B² (1) from Aspergillus fumigatus Fres and we have reported the isolation and structure of the novel peroxide verruculogen¹ (2) from Penicillium verruculosum. Yamazaki² reported the

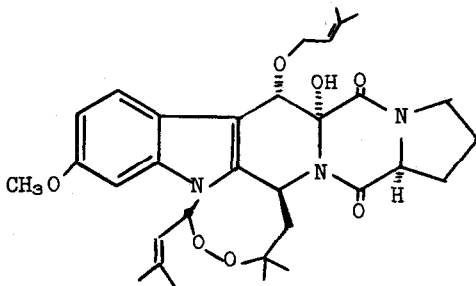


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isolation of another active metabolite from A. fumigatus, $C_{32}H_{41}N_3O_7$, with tremorgenic properties, which he called fumitremorgin A. We have recently reisolated fumitremorgin A and wish to report that x-ray diffraction has shown it to have structure 3. Fumitremorgin A was isolated from Aspergillus fumigatus and had identical physical



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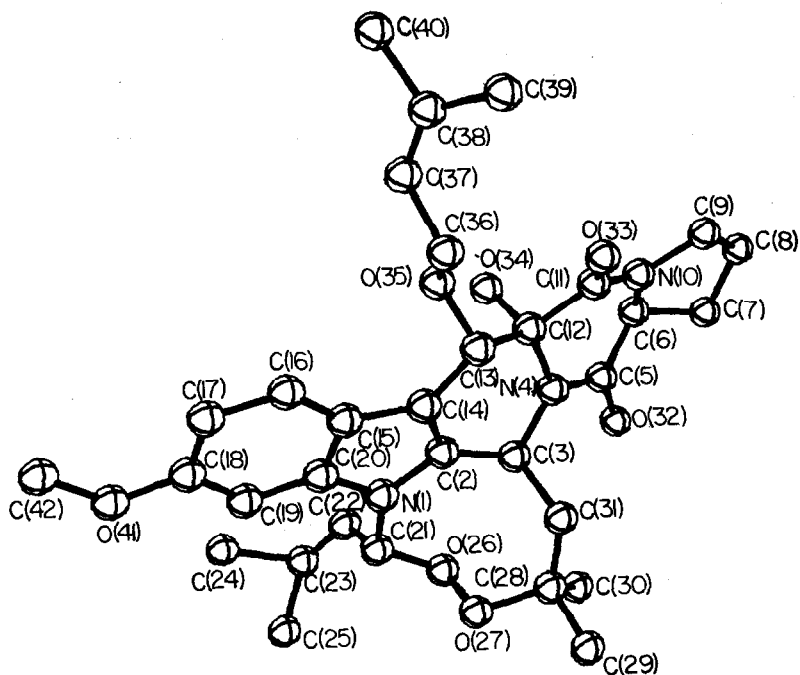
properties with those previously published for fumitremorgin A² and was identical on TLC to an authentic sample.³

The material crystallized in the common chiral space group $P_{2_1}^2$ with $a = 26.862(2)$, $b = 15.718(2)$ and $c = 7.412(1)$ Å and four molecules of $C_{32}H_{41}N_3O_7$ per unit cell. All diffraction maxima with $2\theta < 114^\circ$ were collected (2456 reflections) and 2195 (89.5%) were considered observed after background, Lorentz and polarization corrections ($F_o \geq 3\sigma(F_o)$). The structure was solved routinely by direct methods⁴ and current residual index is 7.6% for the observed reflections. Bond distances and angles agree well with generally accepted values. The figure shows a computer generated drawing of the final x-ray model. The absolute configuration has not been determined in this work.

The structure (3) is best described as the verruculogen (1) structure extended by a five carbon mevalonate derived unit

attached to the secondary alcohol. The unusual, non-endoperoxide link, first found in verruculogen, is present in fumitremorgin A. While this peroxide arises most plausibly from the hydroperoxide we have not yet been able to detect any hydroperoxide.

Since the relative stereochemistry of fumitremorgin A and verruculogen are identical, fumitremorgin B most likely has the same stereochemistry since it occurs in the same isolates with verruculogen and fumitremorgin B.



REFERENCES

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2. M. Yamazaki, K. Susago, and K. Miyaki, J.C.C. Chem. Comm., 408 (1974).
3. An authentic sample of funitremorgin A was kindly provided by Dr. Yamazaki.
4. G. Germain, P. Main and M.M. Woolfson, Acta Cryst., **B24**, 274 (1970).