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STRUCTURE OF CLADOFULVIN

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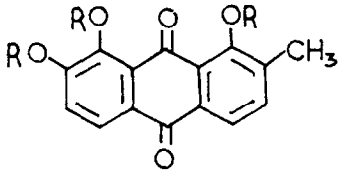
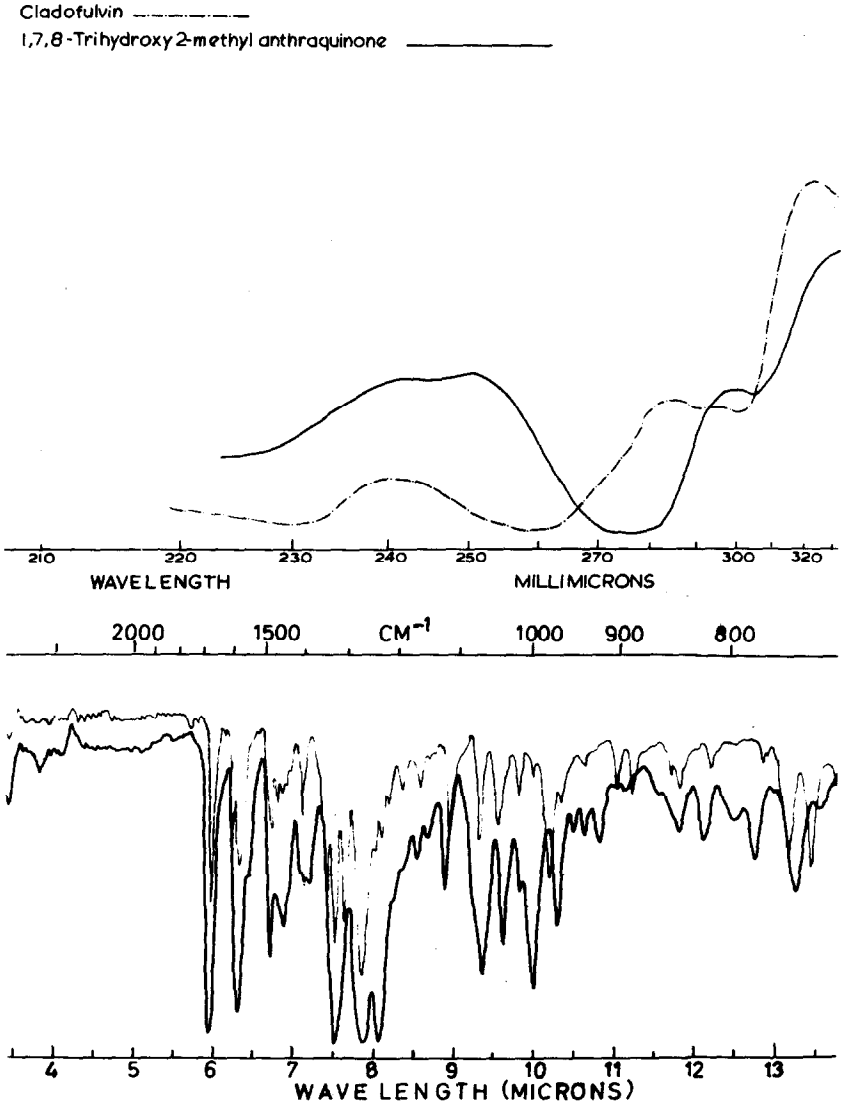
Agosti et al.[1], isolated an anthraquinone pigment as a metabolic product of a wild strain of the fungus Cladosporium fulvum and named it Cladofulvin. Based on elemental analysis, spectral properties and degradation experiments, it was assigned the structure of 1,7,8-trihydroxy-2-methylanthraquinone (I).



(I) R = H

(II) R = CH_3

In connection with the synthesis of morindone, Simonsen[2] had earlier prepared 1,7,8-trimethoxy-2-methylanthraquinone (II). Agosti et al.[1], did not compare the methyl ether of cladofulvin with the above synthetic sample for confirming the structure they proposed for cladofulvin. We have now prepared the synthetic methyl ether according to the procedure of Simonsen viz., condensation of 3,4-dimethoxy phthalic anhydride with o-cresol and cyclisation



1. Cladofulvin trimethyl ether
2. 1,7,8-Trimethoxy 2-methyl anthraquinone

of the resulting benzoyl benzoic acid using concentrated sulphuric acid, and final methylation since the cyclisation under these conditions caused some partial demethylation resulting in the formation of a mixture. The complete methyl ether (II) thus obtained had a m.p. 209-10° agreeing with the report of Simonsen[2]. A sample of cladofulvin trimethyl ether was kindly supplied to us by Dr. C.E. Stickings from Professor J.H. Birkinshaw's collection and a direct comparison between the two samples could be made. It was observed that though they melted near about the same temperature, their mixed m.p. was considerably depressed indicating thereby that they were not identical. Further proof for their nonidentity was provided by a comparison of their UV as well as IR spectra (see chart for latter). Their behaviour in TLC also supported this conclusion. Natural cladofulvin trimethyl ether had R_f 0.3* whereas the synthetic 1,7,8-trimethoxy-2-methyl anthraquinone had R_f 0.8. From these observations it may be concluded that cladofulvin could not have the structure (I).

Simonsen did not prepare the free hydroxyanthraquinone corresponding to the trimethyl ether. This demethylation has now been carried out by refluxing with aqueous HBr (48%) and acetic acid for 12 hr. The trihydroxy compound formed orange needles decomposing above 315°. Cladofulvin, which was orange red, decomposed above 310°. The synthetic

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* Solvent: benzene-ethylacetate (3:1)

trihydroxy compound formed a triacetate, yellow cubes from methanol, m.p. 204-6°. The triacetate of cladofulvin had a m.p. 185-6°. Since only a very small quantity of natural cladofulvin was available to us, only the spectral comparison between synthetic 1,7,8-trihydroxy-2-methylanthraquinone and cladofulvin could be carried out, which indicated that they were not identical (see chart for UV comparison). The two compounds also showed difference in TLC, the synthetic sample moving slightly faster. These evidences further confirm the conclusion that cladofulvin is not 1,7,8-trihydroxy-2-methyl anthraquinone (I).

REFERENCES

1. G. Agosti, J.H. Birkinshaw and P. Chaplen, Biochem. J. 85, 528 (1962).
2. J.L. Simonsen, J. Chem. Soc. 125, 721 (1924).