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AN ALTERNATIVE STRUCTURE FOR BOTRALLIN

A METABOLITE OF BOTRYTIS ALLII

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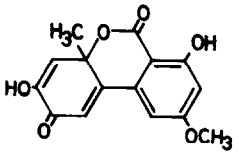
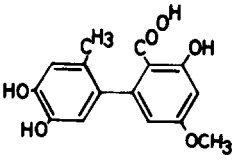
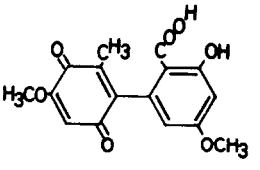
In the course of our investigations on the metabolites of Alternaria kikuchiana Tanaka, two phenolic compounds were newly isolated from the culture medium and identified as dehydroaltenusin (I) and altenusin (II)[1] by physical and chemical data by the authors (K.K.,H.A and M.N.). During this investigation, we found that physical chemical properties of (I) were almost the same as those of botrallin, a metabolite recently isolated from Botrytis allii and proposed as (III_a) by one of the authors (J.C.O.)[2]. Their close resemblance prompted us to reexamine the structure of botrallin and its reduction product and from the following investigation, the latter was found to be (IV_b) instead of (IV_a) and consequently, the former is revised from (III_a) to (III_b).



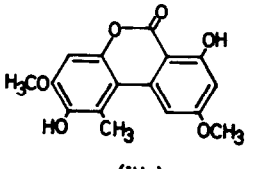
(I)



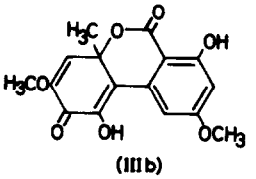
(II)



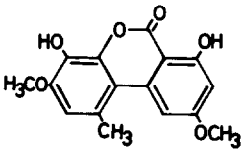
(IIIa)



(IVa)

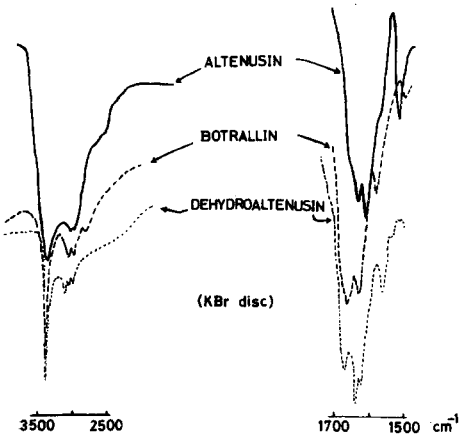


(IIIb)



(IVb)

As shown in the summarized NMR data (Table), botrallin showed the signals at δ 7.23 and 11.36, which were assigned to a phenolic and a carboxylic OH, and dehydroaltenusin (I) also provided the signals due to an enolic and a hydrogen-bonded phenolic OH at δ 7.41 and 11.23, respectively. The signal of the methyl group (δ 1.77) of botrallin was in accordance with



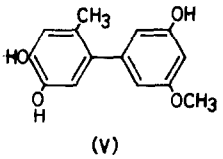
that of the tertiary methyl group (δ 1.76) of (I) and the chemical shifts of the remaining protons also resembled closely to those of (I). Furthermore, the presence of an α-hydroxydienone moiety and a hydrogen-bonded lactone in botrallin was supported by comparison of its IR spectrum with those of (I) and (II). Treatment of (I) with zinc-powder in acetic acid in the same manner as was reported with botrallin[2] gave a product $C_{14}H_{14}O_4$(V) which was identical with the decarboxylated product of (II) in NMR, UV, MS spectra and on tlc. This fact indicates that such p-quinol type lactone as dehydroaltenusin (I) was easily reduced to altenusin (II) involving the opening of the lactone ring and then yielded (V) with loss of carbon dioxide. The facts that botrallin dissolved very slowly in aq. $NaHCO_3$ solution and was unstable in alkaline media strongly indicate that botrallin possesses a hydrogen-bonded lactone (III_b) but not a free carboxyl and a p-quinol (III_a).

COMPOUND	CHEMICAL SHIFTS (δ)
(I)#	1.76 (3H,s), 3.95 (3H,s), 6.33 (H,s), 6.74 (H,s), 6.67 and 6.77 (1H each,d,J 2.4 Hz) 7.41 and 11.23 ($1H^{\dagger}$ each)
(II)¶	1.77 (3H,s), 3.83 (3H,s), 6.60 (H,s), 6.68 (H,s), 6.21 and 6.43 (1H each,d,J 2.4 Hz)
(III_b)#	1.77 (3H,s), 3.80 (3H,s), 3.90 (3H,s), 6.14 (H,s), 6.54 and 7.34 (1H each,d,J 2.4 Hz) 7.23 and 11.36 ($1H^{\dagger}$ each)
(IV_b)§	2.70 (3H,s*), 3.85 (3H,s), 3.93 (3H,s), 6.78 and 7.36 (1H each,d,J 2.4 Hz) 6.90 (H,s*) 7.22 ($H^{\dagger}$), 12.58 ($H^{\dagger}$)
(VI)#	2.82 (3H,s*), 3.87 (3H,s), 3.93 (3H,s), 6.78 (2H,br.*), 6.57 and 7.27 (1H each,d,J 2.4 Hz) 11.95 ($H^{\dagger}$)
(VII)#	2.40 (3H,s), 2.42 (3H,s), 2.82 (3H,s*), 3.92 (3H,s), 3.95 (3H,s), 6.78 (H,s*) 6.76 and 7.62 (1H each,d,J 2.4 Hz)

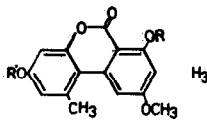
$CDCl_3$, ¶ $CDCl_3/CD_3COCD_3$, § Py-d_5, * long range coupling, † exchangable with D_2O

On the other hand, as described in the earier paper[2], the reduction product of botrallin showed the IR spectrum of a chelated δ-lactone (ν^{KBr}1650 cm^{-1}) and substituted aromatic system (ν^{KBr}1623, 1600 and 1572 cm^{-1}). In its NMR spectrum, the presence of a long range coupling (J 0.17 Hz) between a singlet proton at δ 6.90 and methyl protons at δ 2.70 indicates that the aromatic proton may be located on the ortho-position of the methyl group and reduction product of botrallin (IV_b) has a skeletal structure analogous to alternariol dimethyl ether (VI) as shown in

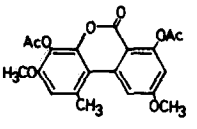
the Table. Acethylation of (IV_b) with acetic anhydride-pyridine afforded a diacetate (VII) m.p. 234 °C, $C_{20}H_{18}O_8$, which showed the UV spectrum closely resembled to that of 3-acetoxy-4',5-dimethoxy-6'-methyl-dibenzo-α-pyrone (VIII). Since no lowfield shift of the proton at δ 6.90 (py-d_5) was observed with acetylation, the acetoxyl group might locate at the meta-position of the aromatic proton (δ 6.93,py-d_5). The facts that one proton of (VII) was found at low-field (δ 7.62) and its chemical shift scarcely affected by changing of solvents (Py-d_5 and $CDCl_3$) may be explained in terms of the steric compression by the bulky methyl group.



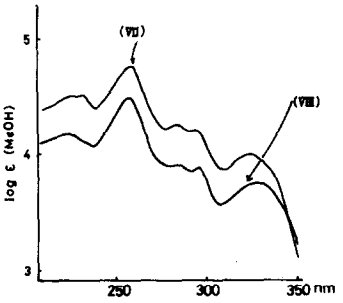
(V)



(VI) R=H,R'=CH_3
(VIII) R=Ac,R'=CH_3
(IX) R=R'=Ac



(VII)



Intramolecular nuclear Overhauser effect was applied on (VII) to confirm this assumption and location of the substituents. On saturation of the C-CH_3 protons at δ 2.82, the signal area for the proton at δ 7.62 increased by 10 % with slightly sharpened shape, which can be attributed to a long range coupling by six bonds, while the proton at δ 6.78 adjacent to the methyl group was decoupled and the signal area for the protons at δ 6.76 and 6.78 increased in all by 10 %. In the same way, on each irradiation of the ring protons at δ6.78 and 7.62, NOE's (8 % each) of the methyl protons were observed. On the other hand, on irradiation of O-CH_3 protons (δ 3.92 and 3.95), the signals for the ring protons at δ 6.76 and 6.78 in all were enhanced about 30 %, while the aromatic proton at δ 7.62 and the methyl protons at δ 2.82 remained unchanged, indicating proximity (ca.1.3 A) of O-CH_3 groups to ring protons at δ 6.76, 6.78 and therefore, O-CH_3 groups on the ring are hindered in their free rotation. These considerations on NOE's results were supported by the facts that the known compound (IX) gave similar NOE as follows. The irradiation of $C_{6'}$-CH_3 enhanced C_6-H and $C_{5'}$-H by 35 and 29 %, respectively. Similarly, on irradiation of $C_{5'}$-OCH_3, the signal area for the C_4-H was enhanced by 19 %. From the data mentioned above, the following conclusions can be drawn on a partial structure of (VII):
(a) biphenyl moiety of (VII) is bounded by δ-lactone ring, (b) O-CH_3 groups and meta-coupled protons (δ 3.92, 3.95, 6.76 and 7.62) are at the position 4', 5, 4 and 6, respectively, on 6'-methyl-dibenzo-α-pyrone, (c) C-CH_3 group and ring proton at δ 6.78 are at the position 6' and 5', respectively, and (d) methyl group at C-6' is very proximate (ca. 1.0 A) to the proton at C-6.

In conclusion, the structure of the reduction product of botrallin should be corrected as (IV_b) and therefore, that of botrallin as (III_b).

As to the biogenesis of botrallin and its relating products, that of alternariol was elucidated by Thomas et al.[3] by tracer experiment, but not yet on the more hydroxylated dervatives as (I), (II) and (III_b). The structural similarity of dehydroaltenusin (I) and botrallin (III_b) demonstrated here is indicative of their biosynthetic derivation from a common polyketide precuosor as alternariol, requiring the oxidative conversion of the substituted resorcinol ring into the corresponding catechol or pyrogallol derivatives.

Acknowledgements: We are grateful to Prof. R. Thomas for a gift of dehydroaltenusin.

References and Footnotes

1) The sample of dehydroaltenusin given by Prof. Thomas was identical with ours in IR, UV, NMR and MS spectra. For structural elucidation see : D. Rogers, D. J. Williams and R. Thomas, Chem. Commun., 1971, 393

2) J. C. Overeem and A. VAN Dijkman, Rec. Trav. Chim. Pays-Bas, 87, 940 (1968)

3) R. Thomas, Biochem. J., 78, 748 (1966)