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CHESTERSIENE, 4-(4-METHOXYPHENOXY)BUTA-1, 2-DIENE: AN ALLENIC ETHER FROM THE FUNGUS *HYPOXYLON CHESTERSII**

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Key Word Index—*Hypoxylon chestersii*; fungal metabolite; allenic ether; chestersiene.

Abstract—Culture solutions of the fungus *Hypoxylon chestersii* contain a new allenic ether which has been identified as 4-(4-methoxyphenoxy)buta-1, 2-diene. The synthesis of the metabolite is described. This is the first report of the natural occurrence of an aromatic allenic ether.

INTRODUCTION

In our previous two papers [1, 2] we have described the isolation of new butenolactones from the fungus *Hypoxylon serpens* (Persoon ex Fries) Kickx and *H. serpens* (Barrons strain). *H. chestersii* (Rogers and Whalley), a recently described species from Wales [3, 4], is considered to be closely related to *H. serpens*; differing from the latter in its possession of ornamented ascospores. We have examined the metabolites produced by this species and have isolated the aromatic allenic ether (**1**).

H. chestersii grows rapidly in a potato dextrose–yeast (PDY) or malt extract medium. The metabolite (**1**) is only produced in PDY and can be isolated by solvent extraction of the medium. Lactones of the type produced by *H. serpens* are not produced by this species.

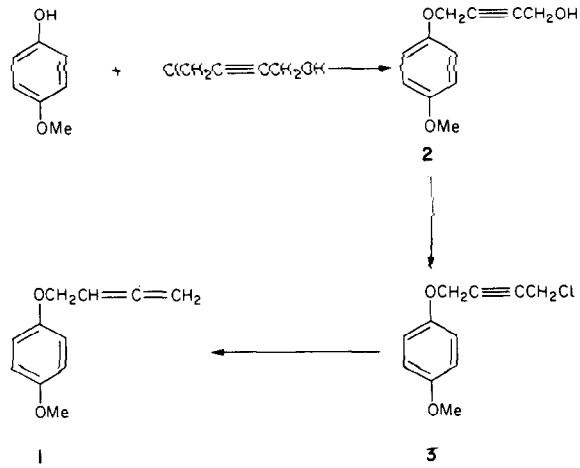
RESULTS AND DISCUSSION

Chestersiene (**1**), $C_{11}H_{12}O_2$, mp 45–47°, was isolated as a colourless crystalline solid after chromatography of the ether extract on silica. The metabolite is best detected on Si gel with iodine; a yellow strain, which turns blue after 5 min, is produced. IR absorption at 1965 cm^{-1} indicated the presence of an allenic group. The MS showed ions at *m/z* 176 $[M]^+$, 161 $[M-Me]^+$ and 124 $[M-C_4H_4]^+$; the latter ion indicated the presence of a four-carbon chain.

The ^1H NMR spectrum gave the general structure. The presence of a methoxy group was confirmed by the absorption at δ 3.9 (3H, *s*, OMe) and the disubstitution pattern on the aromatic ring was identified as *para* by the single absorption at δ 6.9 (4H, *s*). Additional absorptions at δ 5.4 (1H, *m*, $-CH=$), 4.55 (2H, *m*, $-OCH_2-$) and 4.9 (2H, *m*, $=CH_2$) account for the remaining protons and lead to the assignment of structure **1**.

The nature of the side-chain was also proved by catalytic reduction over PtO_2. The low melting product no longer showed allene absorption in the IR and its mass spectrum (*m/z* 180 $[M]^+$) showed a prominent ion at *m/z* 124 corresponding to the loss of a C_4H_8 fragment. Also, in the ^1H NMR spectrum the ring and the methoxyl absorptions at δ 6.84 (4H, *s*) and 3.66 (3H, *s*) were retained but the remaining absorptions at δ 3.8 (2H, *t*, $-OCH_2$), 1.32 (4H, *m*, $-CH_2-CH_2-$) and 0.83 (*t*, –Me) clearly indicated the presence of a butyloxy group and identified the reduced compound as 1-butyloxy-4-methoxybenzene.

Final proof of the structure was established by the synthesis of **1** and its reduction product, 1-butyloxy-4-methoxybenzene. Chestersiene (**1**) was synthesized (Scheme 1) via the acetylenic ether. 1-Chloro-4-hydroxybut-2-yne was reacted with 4-methoxyphenol in the presence of base [5]; the resulting acetylenic ether (**2**) was chlorinated with thionyl chloride and the chloro-acetylenic ether (**3**) was reduced to chestersiene with either lithium aluminium hydride [6] or with a zinc–copper couple [7]. A second synthesis



Scheme 1. Chemical synthesis of 1.

*Part 20 in the series "Metabolites of the Higher Fungi". For Part 19 see ref. [1].

was attempted; 1-chloro-4-hydroxybut-2-yne was reduced with lithium aluminium hydride and the resulting allenic alcohol was brominated with triphenylphosphite dibromide [8]. Attempts to react the allenic bromide with 4-methoxyphenol, however, failed to yield any of the required product.

1-Butyloxy-4-methoxybenzene was synthesized by reacting butyl iodide with 4-methoxyphenol. The synthesized compounds have the same ^{1}H NMR, IR and UV spectra as the natural product (**1**) and the reduced natural product.

In the ^{1}H NMR spectrum of chestersiene, long-range coupling occurs between the protons of the butadienyloxy group. The spectrum shows the features of an A_2BX_2 system. Both methylene protons show identical splitting and consist of a doublet, each component of which comprises a triplet. The methyne proton appears as a symmetrical pentet [9, 10].

The allenic function is not common among natural products, the largest group of compounds are the long-chain polyacetylenes isolated from the basidiomycetes [11, 12]. Fucoxanthin, fucoxanthinol, neoxanthin, de-epoxineoxanthin and paracentrone represent a group of allenic carotenoids [13] and 5, 6-octadecadienoic acid [14] and 8-hydroxy-5,6-octadienoic acid [15] (from seed oils) represent allenic acids. The pupa of the male dried bean beetle contains an allenic ester identified as methyl *n*-tetradeca-*trans*-2,4,5-trienoate [16] and the grasshopper *Romalea microptera* produces an allenic terpene [17]. An allenic steroid, 24-ethyl-$\Delta^{5,24(28)28}$ cholestatriene-3β-ol has been isolated from the sponge *Callysporangia diffusa* [18] and a new cyclic brominated allenic ether, laurallene has recently been identified from the marine red alga *Laurencia nipponica yamada* [19]. To our knowledge aromatic allenic ethers have not been isolated previously from a natural source.

EXPERIMENTAL

Mps were determined on a Kofler hot-stage apparatus; ^{1}H NMR: JEOL JNM-MH-100, TMS as int. standard; TLC and CC: Merck kieselgel $PF_{256+366}$; prep. TLC: Si gel (16 g) on 20 × 20 cm glass plates.

Isolation of chestersiene (**1**). *H. chestersii* (IMI 22810) was cultured in Thompson bottles (2 l.) in PDY medium. After 8 weeks the soln was filtered from the colourless mycelium. The filtrate (18 l.) was extracted with Et_2O(× 3), the extract dried (Na_2SO_4), and evaporated to yield a pale brown oil (1.12 g) which slowly solidified. The solid was dissolved in a mixture of petrol (bp 60–80°)–Et_2O–HOAc (90 : 10 : 1) and the soln applied to a column of Si gel (2 × 40 cm). Development of the column with the same solvent mixture gave several fractions. The first fraction yielded an oil (155 mg) which crystallized overnight. Recrystallization of the solid from petrol (bp 60–80°) yielded **1** as colourless plates (60 mg), mp 45–47°. (Found: C, 75.0; H, 6.76. $C_{11}H_{12}O_2$ requires C, 75.0; H, 6.8%.) IR ν_{max} 1965 cm^{-1}; UV λ_{max} (cyclohexane) nm (log ϵ): 204 (3.85), 227 (3.94), 290 (3.37).

Catalytic reduction of chestersiene. Chestersiene (38 mg) was dissolved in absolute EtOH and hydrogenated over PtO_2 until absorption of H_2 was complete. The soln was filtered and evaporated to yield an oily residue which slowly crystallized. Recrystallization from MeOH gave 1-butoxy-4-methoxybenzene as colourless plates, mp 24–25° (32 mg), showing ^{1}H NMR, and IR identical with an authentic sample [20].

1-Chloro-4-hydroxybut-2-yne. This was prepared according to ref. [21].

4-Hydroxy-1-(4-methoxyphenoxy)but-2-yne (**2**) *and 4-chloro-1-(4-methoxyphenoxy)but-2-yne* (**3**). These were prepared according to ref. [5] giving **2** as a green oil, bp 166° (1 mm), ^{1}H NMR ($CDCl_3$): δ 4.0 (3H, *s*), 4.58 (2H, *s*) 4.85 (2H, *s*), 7.05 (4H, *d*, J = 10 Hz) (Found: 68.5; H, 6.4. $C_{11}H_{12}O_3$ requires C, 68.65; H, 6.25%), and **3** as a pale green oil, bp 146° (1 mm) (Found: C, 62.9; H, 5.2; Cl, 16.9. $C_{11}H_{11}O_2Cl$ requires C, 62.7; H, 5.2; Cl, 16.9%.) ^{1}H NMR ($CDCl_3$): δ 3.68 (3H, *s*), 4.06 (2H, *t*, J = 2 Hz) 4.56 (2H, *t*, J = 2 Hz), 6.74 (4H, *s*).

4-(4-Methoxyphenoxy)-buta-1, 2-diene (chestersiene) (**1**). (a) To a stirred soln of $LiAlH_4$ (2.32 g) in dry Et_2O (90 ml), was added 4-chloro-1-(4-methoxyphenoxy)-but-2-yne (6.0 g) in dry Et_2O (50 ml) over 30 min. The mixture was refluxed 17 hr. The excess hydride was destroyed (EtOAc) and the reaction mixture strongly acidified with HCl (10%). The aq. layer was separated and extracted with Et_2O (3 × 3 ml). The combined Et_2O extracts were dried (K_2CO_3), the Et_2O soln evaporated and the resulting oil dissolved in a mixture of petrol (bp 60–80°)–Et_2O–HOAc (40 : 10 : 1) (10 ml), and applied to a column of Si gel (63 × 4 cm). Development of the column with the same solvent mixture yielded four fractions. Fraction (2) yielded an oil which crystallized overnight. Recrystallization from petrol (bp 60–80°) gave **1** as plates mp 45–47° (0.5 g). (Found: C, 75.3; H, 6.8. $C_{11}H_{12}O_2$ requires C, 75.0; H, 6.8%.) UV λ_{max}^{EtOH} nm (log ϵ): 204 (3.78), 227 (3.94), 290 (3.99).

(b) To a mixture of Cu powder (3.5 g) and Zn powder (4.0 g) in boiling absolute EtOH (25 ml) was added 4-chloro-1-(4-methoxyphenoxy)-but-2-yne (10 g) in absolute EtOH (30 ml). The mixture was refluxed 1.5 hr. The soln was cooled, centrifuged and evaporated under vacuum to yield a brown oil which was dissolved in Et_2O. The Et_2O soln was washed with H_2O, dried, evaporated and the residual oil applied to a column of Si gel (30 × 1.5 cm). Elution of the column with the solvent system petrol–Et_2O–HOAc (40 : 10 : 1) gave several fractions. The first fraction, after removal of the solvent, gave an oil (2.1 g) which slowly solidified to yield **1** mp 45–47° after recrystallization from petrol.

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