

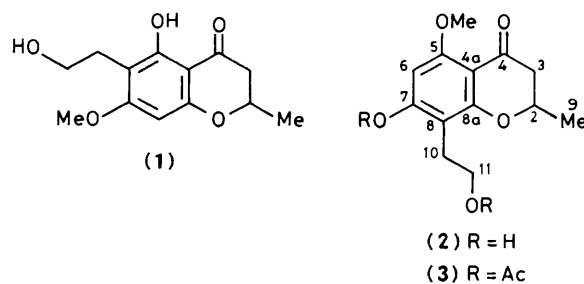
Structural Revision and Synthesis of LL-D253 α : a Chromanone Metabolite of *Phoma pigmentivora*

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LL-D253 α , a chromanone metabolite of *Phoma pigmentivora*, has been shown by analysis of the ^1H -coupled ^{13}C n.m.r. spectrum and by synthesis to be 7-hydroxy-8-(2-hydroxyethyl)-5-methoxy-2-methylchromanone.

LL-D253 α was first isolated from *Phoma pigmentivora* and was assigned the chromanone structure (1) on the basis of spectroscopic and degradative studies.¹ It has also been isolated along with a number of related co-metabolites from *Phoma violacea* and *Sclerotinia fructigena*.² We now report ^{13}C n.m.r. studies on LL-D253 α , carried out as a preliminary to biosynthetic labelling experiments,³ which necessitate revision of the structure to (2) on the basis of a full analysis of the fully ^1H -coupled ^{13}C n.m.r. spectrum of LL-D253 α diacetate (3). This has been confirmed by unambiguous syntheses of both structures (1) and (2).



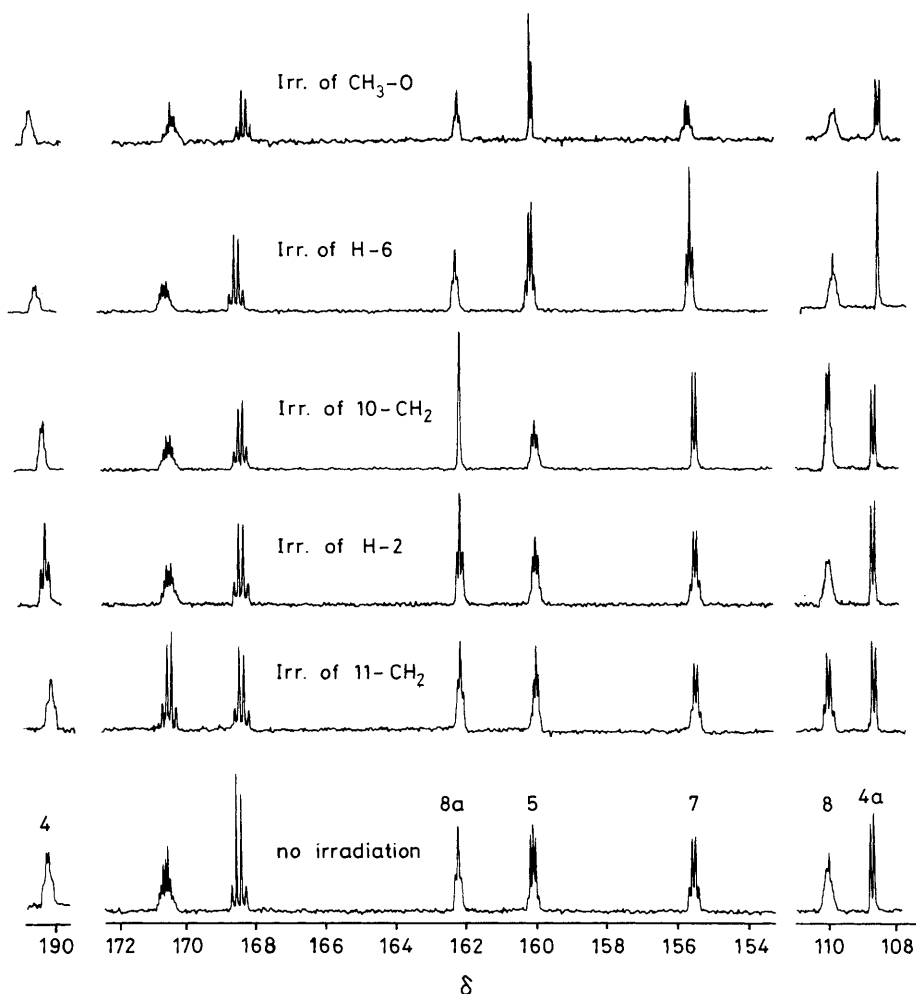


Figure 1. The high-frequency region of the fully ^1H -coupled 200 MHz ^{13}C n.m.r. spectrum of LL-D253 α diacetate, and results of selective low-power ^1H decoupling experiments.

Figure 1 shows the high frequency region of the fully ^1H -coupled ^{13}C n.m.r. spectrum of LL-D253 α diacetate (**3**) and the results of a series of specific low-power decoupling experiments.⁴ All the aromatic carbons give characteristic multiplet patterns.[†] The hydroxyethyl side chain must be placed at C-8 rather than C-6 of the chromanone skeleton as irradiation of the benzylic methylene hydrogens (10- CH_2) and H-2 respectively caused the multiplet resonance at δ 162.1 to sharpen to a broad singlet and a sharp triplet (Figure 1). These results, along with the chemical shift, indicate that this resonance must therefore be assigned to C-8a, showing 3-bond couplings to 10- CH_2 and H-2. Similarly the phenolic acetate must be placed at C-7 as irradiation of 10- CH_2 and H-6 respectively change the quartet at δ 155.1 to a doublet and a triplet; and the methoxy substituent must be placed at C-5 as the quintet at δ 160.0 collapses to a quartet and doublet respectively on irradiation of H-6 and OCH_3 . The complex multiplet at δ 110.0 is assigned to C-8 as it sharpens to a quartet on irradiation of either 10- CH_2 or 11- CH_2 . It also sharpens slightly and shows an intensity increase on irradiation of H-6 due to removal of the expected 3-bond coupling. C-4a also shows a 3-bond coupling to H-6. The carbon-hydrogen couplings revealed by these experiments are sum-

[†] C-6 gives a doublet [$J(^{13}\text{C}-^1\text{H})$ 126 Hz] and exhibits no long-range couplings.

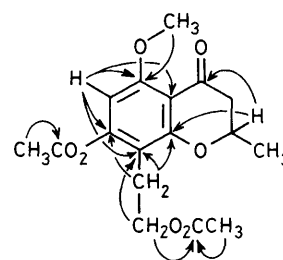
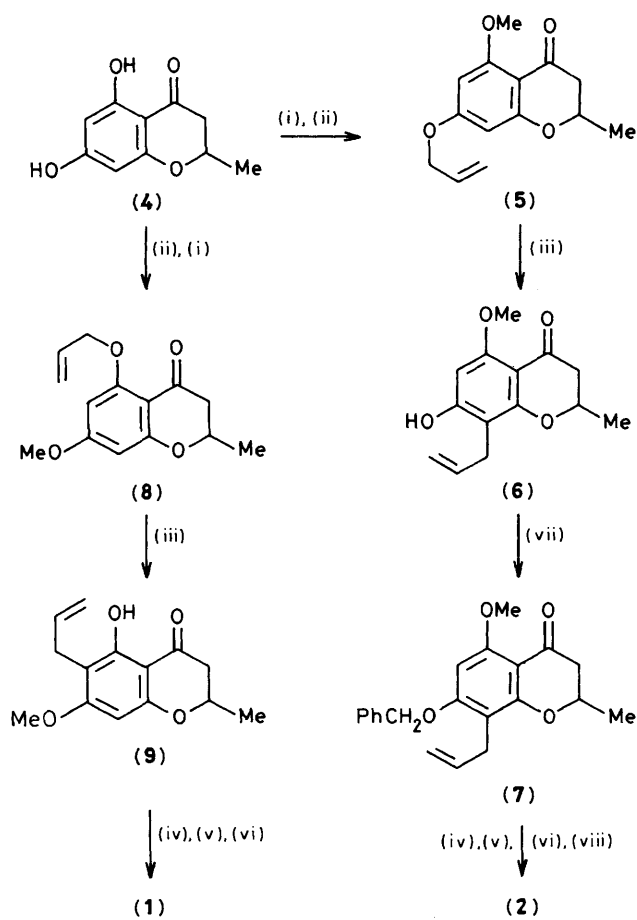


Figure 2. Long range ^1H - ^{13}C couplings in LL-D253 α diacetate selectively removed by low-power ^1H decoupling experiments.

marised in Figure 2. Although these effectively define structure (**2**) for LL-D253 α , confirmatory evidence was provided by unambiguous syntheses of both (**1**) and (**2**) from 5,7-dihydroxy-2-methylchromanone (**4**)⁵ as outlined in Scheme 1. Allylation of the non-chelated hydroxy group on C-7 followed by methylation gave (**5**), which on heating to melting underwent a Claisen rearrangement to furnish (**6**).[‡] In

[‡] There is much precedent in the literature for Claisen rearrangement of 7-allyl ethers in chromone and chromanone systems to give mainly or exclusively the 8-allyl derivatives.⁶



Scheme 1. Reagents and conditions: (i) $\text{H}_2\text{C}=\text{CHCH}_2\text{Br}$, K_2CO_3 ; (ii) MeI , K_2CO_3 ; (iii) heat; (iv) OsO_4 ; (v) NaIO_4 ; (vi) NaBH_4 ; (vii) PhCH_2Br , K_2CO_3 ; (viii) H_2 , Pd(C) .

the presence of the free 7-hydroxy group all attempts to cleave the double bond oxidatively gave intractable mixtures. However, after protection as the benzyl ether (7), osmium tetroxide oxidation to the vicinal diol, periodate cleavage, and borohydride reduction of the resultant aldehyde, compound (2) was obtained in acceptable overall yield [16% from (4)] on hydrogenolysis of the benzyl protecting group. This was identical in all respects to natural LL-D253 α . Structure (1) was obtained from (4) by methylation followed by allylation to give (8), which underwent Claisen rearrangement to (9). The allyl moiety was cleaved to the hydroxyethyl moiety as above without protection of the chelated hydroxy group being necessary. The overall yield of (1) from (4) was 44%. In contrast to LL-D253 α , compound (1) was readily soluble in CDCl_3 and its ^1H n.m.r. spectrum showed the presence of a chelated hydroxy proton at δ 12.17, whereas the ^1H n.m.r. spectrum of LL-D253 α in CDCl_3 showed that no chelated hydroxy group was present.

The ^1H -coupled ^{13}C n.m.r. spectra of (1) and a third isomer have been obtained and will be reported in full elsewhere.

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