

The Structure of Americanin A

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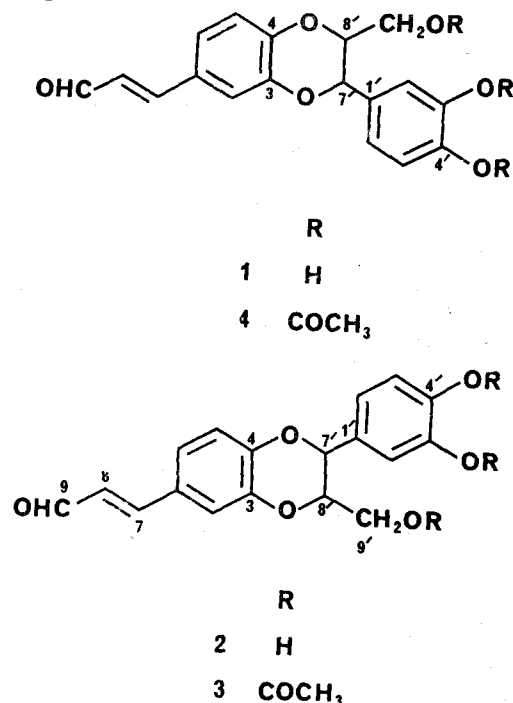
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Abstract—The structure of the neolignan americanin A was confirmed to be **2**, through the application of the Selective INEPT NMR technique. Complete and unambiguous proton and ¹³C-NMR assignments are provided.

Keywords—Benzodioxane lignan • americanin A • 2D-NMR

Americanin A is a neolignan obtained from the roots of *Phytolacca americana* L. (Phytolacaceae) whose structure was proposed to be **1**, based on spectroscopic evidence.¹⁾ In 1981, this structure was revised to **2**, because americanin A provided the starting material for the partial synthesis of a derivative of the flavonolignan silandrin²⁾, and very recently³⁾, during the course of these studies, supporting chemical evidence for this structure revision has been presented. The interest of one of our groups (Woo *et al.*) in the constituents of *P. americana* led to this collaboration to determine spectroscopically whether **1** or **2** is the correct structure of americanin A. The strategy used to establish the structure was basically the same as that described for the structure elucidation of coumarinolignans^{4,5)}, since both moieties contain the 1,4-benzodioxane nucleus. For solubility reasons all studies were conducted on the triacetate derivative of americanin A.

The homonuclear COSY spectrum of americanin A triacetate (Fig. 1) revealed that the doublet of doublets at 7.14 ppm (H-6) is *ortho* coupled to the doublet at 6.99 ppm (H-5) with a coupling constant of 8.4 Hz, and is also *meta* coupled to the doublet at 7.21 ppm (H-2) with



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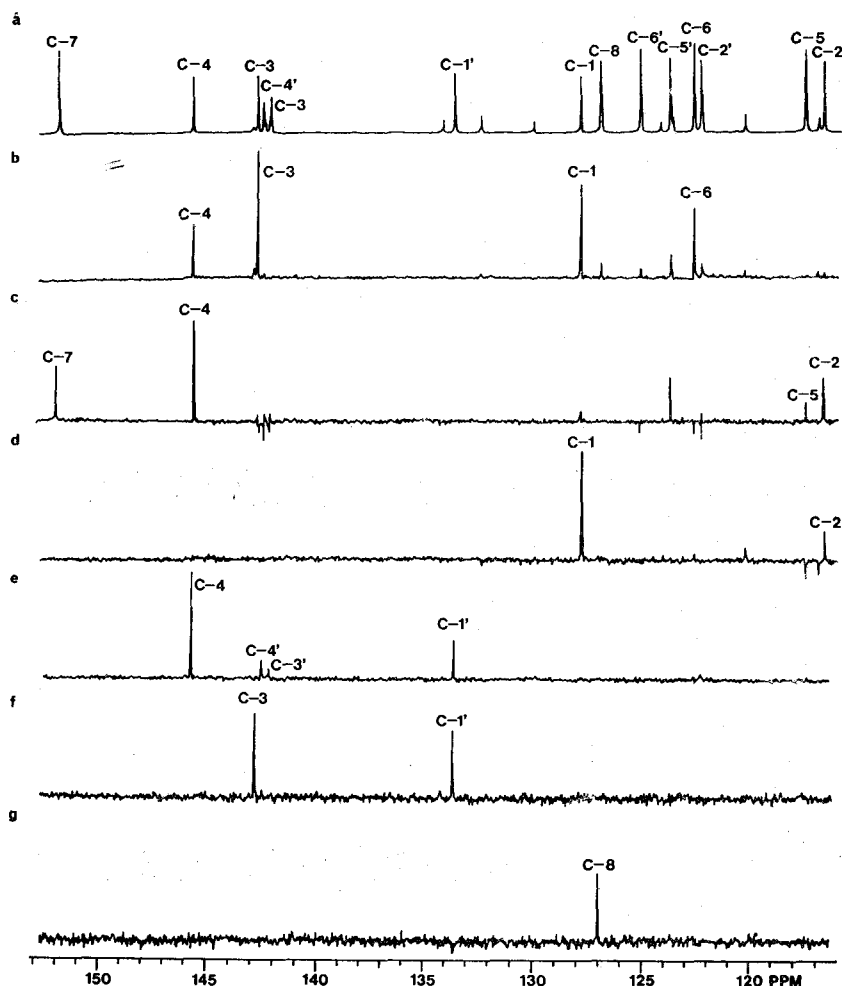


Fig. 2. Downfield region of the ^{13}C -NMR spectrum of americanin A triacetate (3). a, Proton noise decoupled spectrum; b-g, SINEPT spectra obtained by irradiation of H-5 ($J=8\text{ Hz}$), H-6 (8 Hz), H-8 (8 Hz), H-7' (1 Hz), H-8' (1 Hz) and H-9 (10 Hz), respectively.

signal at 145.7 ppm was assigned to C-4, which is three-bond coupled to H-6, and the next most intense signal at 151.9 ppm was assigned to C-7 for the same reason.⁽⁷⁾ The enhanced signals at 116.7 and 117.5 ppm were assigned to C-2 and -5, respectively, due to three-bond and two-bond coupling to H-6. The signal observed at 123.7 ppm which was assigned to C-2', C-5' or C-6' was regarded as a residual signal due to one of the ^{13}C satellites of either H-2', H-5' or H-6'.

Irradiation of H-8 using the same delay time as for the irradiation of H-6 and H-5 resulted

in the enhancement of two signals. The intense signal at 127.9 ppm was assigned to C-1, which is three-bond coupled to H-8. The small enhancement of the carbon signal at 116.7 ppm (C-2) indicated that this carbon is also coupled to H-8, but with a smaller coupling constant.

Irradiation of H-7' with $J_{\text{CH}}=1\text{ Hz}$ resulted in the enhancement of four signals. The most intense signal, at 145.7 ppm assigned to C-4, was also the resonance found to be the most enhanced when H-6 was irradiated, thus strongly suggesting that 3 is the correct structure of americanin A triacetate rather than structure 4.

The next most intense signal, at 133.6 ppm, was assigned to C-1' which is two-bond coupled to H-7'. The same signal (C-1') was also enhanced in coumarinolignans whenever H-7' was irradiated.⁴⁾ Two small signals at 142.5 and 142.2 ppm, were assigned to C-4' and C-3', respectively, based on their intensity. Although C-4' is five-bond coupled to H-7', according to a model compound-toluene, the value of $^5J_{CH}$ is larger than $^4J_{CH}$. It therefore seemed reasonable to attribute the signal at 142.5 ppm to C-4', since the J_{CH} value used in this experiment was 1 Hz.

Irradiation of H-8' with $J_{CH}=1$ Hz resulted not only in the enhancement of C-1' at 133.6 ppm, but also in the enhancement of the C-3 signal at 142.7 ppm, that is the same carbon (C-3) as did irradiation of H-5. The suggestion that **3** is the correct structure for americanin

A triacetate is therefore further confirmed. Due to the overlap of H-2', H-5' and H-6', it was difficult to assign these protons. However, irradiation of H-7' with $J_{CH}=6$ Hz resulted in the enhancement of the signals at 125.1 and 122.3 ppm, which were assigned to C-6' and C-2', respectively.

In order to assist in the assignment of C-8, the aldehyde proton (H-9) was irradiated with $J_{CH}=10$ Hz. The only carbon signal observed at 127.0 ppm was thus assigned to C-8 which is two-bond coupled to H-9. It is established⁸⁾ that large, positive two-bond coupling constants can be observed for α,β -unsaturated aldehydes. CSCM 1D experiments⁽⁹⁾ were used to initially assign C-7' and C-8' in **3**. Thus irradiation of the proton at 5.03 ppm*, which from its chemical shift, multiplicity and the COSY spectrum must be H-7' led to a specific enhancement of the

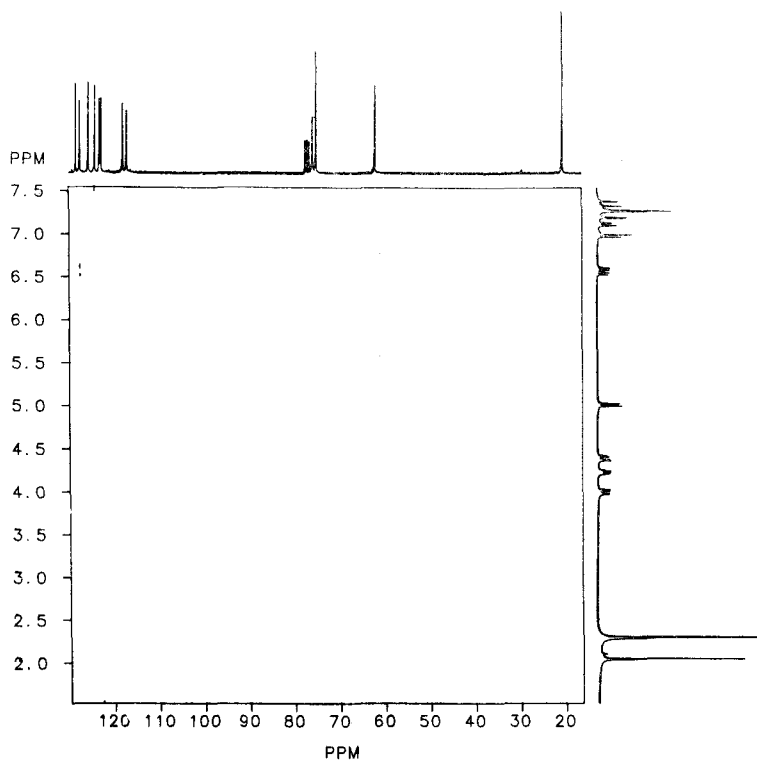


Fig. 3. ^1H - ^{13}C Correlation spectrum for americanin A triacetate (**3**) in CDCl_3 .

* Irradiations were conducted 75 Hz upfield and downfield of the center of the proton resonances with identical results in terms of enhancement.

Table II. ^{13}C -NMR spectroscopic data for americanin A and its triacetate

Americanin A				Americanin A triacetate			
Carbon	(DMSO- d_6) ^a	(DMSO- d_6) ^a	(CDCl ₃) ^b	Carbon	(DMSO- d_6) ^a	(DMSO- d_6) ^a	(CDCl ₃) ^b
		initial assignments	revised assignments			initial assignments	revised assignments
1	127.6 ^c	128.1 (s)	127.9(s)	4'	145.9 ^e	142.1 ^g (s)	142.5(s)
2	116.8	116.9 ^f (d)	116.7(d)	5'	115.5 ^d	123.9 ^h (d)	123.7(d)
3	143.5	142.7 ^g (s)	142.7(s)	6'	118.9	126.0 (d)	125.1(d)
4	146.6	145.8 (s)	145.7(s)	7'	76.1	75.4 (d)	76.0(d)
5	117.3	117.5 ^f (d)	117.5(d)	8'	78.1	74.3 (d)	75.8(d)
6	122.6	123.0 ^h (d)	122.6(d)	9'	60.1	62.0 (t)	62.0(t)
7	126.8	127.2 (d)	151.9(d)	<u>COCH</u> ₃		168.0 (q)	167.6(q)
8	153.0	152.6 (d)	127.0(d)	<u>COCH</u> ₃		168.0 (q)	167.6(q)
9	194.0	193.9 (d)	193.2(d)	<u>COCH</u> ₃		169.8 (q)	169.9(q)
1'	127.2 ^c	134.2 (s)	133.6(s)	<u>COCH</u> ₃		20.2 (q)	20.4(q)
2'	115.0 ^d	123.0 (d)	122.3(d)	<u>COCH</u> ₃		20.2 (q)	20.4(q)
3'	145.3 ^e	142.5 ^g (s)	142.2(s)	<u>COCH</u> ₃		20.2 (q)	20.4(q)

a) Data are from reference 1.

b) Recorded at 90.8 MHz using TMS as an internal standard.

c-h) Assignments may be reversed.

signal at 76.0 ppm. On the other hand irradiation at 4.24 ppm* (H-8') only enhanced the signal at 75.8 ppm which could therefore be assigned to C-8'. Finally, direct confirmation of the assignment of all the protonated carbon atoms was achieved through a 2D-heteronuclear chemical shift correlation experiment (Fig. 3).

Comparison of our data with the literature ^{13}C -NMR data of americanin A and its triacetate (3) is shown in Table II. The revised^{2,3} structure of americanin A is therefore confirmed as being that shown in 2.

(Received Feb. 25, 1987 : Accepted Mar. 25, 1987)

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