

Splendidin, a New *trans*-Clerodane from *Salvia splendens*

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Splendidin, isolated from *Salvia splendens* (Labiatae) has been shown by ^1H and ^{13}C n.m.r. determinations to be 1,11-diacetoxy-15,16-epoxy-*trans*-cleroda-2,13(16),14-trieno-12,17:19,18-dilactone (2).

We have reported¹ the isolation and X-ray structure determination of salviarin (1), a *trans*-clerodane, obtained from *Salvia splendens* (Labiatae). Further examination of this species has yielded another diterpenoid, splendidin

oxygen functions were secondary in character. The ^{13}C n.m.r. spectrum also revealed the presence of two further methylene carbons, two doublet olefinic resonances, three further methine signals, and two quaternary

^{13}C and ^1H n.m.r. signals of splendidin (2) and derivatives (4) and (5)

Carbon atom	δ_{C}				δ_{H}		
	(2)	SFORD multiplicity	(4)	SFORD multiplicity	(2)	(4)	(5)
1	75.9	d	78.3	d	5.51 d of t	5.40 d of t	5.21 t
2	122.3	d	122.2	d	5.90 d of d	5.99 d of t	c
3	128.9	d	128.9	d	5.70 d of d	5.70 d of d	c
4	51.3	d	51.6	d	2.86 q	2.92 q	2.73 m
5	40.0 ^a	s	40.9 ^a	s			
6	31.6	t	30.5	t	1.46 t of t	c	1.46 t of d
					1.85 d	c	1.85 m
					1.98 d	c	c
7	19.4	t	20.2	t	2.48 m	c	2.40 m
8	50.1	d	46.9	d	2.79 m	2.04 d,d,d,	2.38 m
9	42.4 ^a	s	42.8 ^a	s			
10	41.4	d	39.5	d	2.52 d	3.03 d	2.34 d
11	71.2	d	67.6 ^b	d	5.39 d	5.22 d	5.35 d
12	66.7	d	67.1 ^b	d	5.87 d	5.32 d	5.85 d
13	121.5	s	122.2	s			
14	108.5	d	109.2	d	6.42 br s	6.42 br s	6.43 br s
15	144.2	d	143.5	d	7.51 br s	7.47 br s	7.50 br s
16	141.7	d	141.7	d	7.42 br s	7.37 br s	7.42 br s
17	170.0 ^b	s	91.1	d		6.38 d, <i>J</i> 9 Hz	
18	174.4 ^b	s	174.4	s			
19	70.5	t	70.9	t	4.16 br d	4.08 br d	3.97 br d
20	19.35	q	18.6	q	4.35 d	4.32 d	4.28 d
Ac	169.1; 169.7; 20.0; 21.8		169.5; 170.4(2); 20.2; 21.2; 21.7		1.07 s	1.05 s	1.06 s
					1.90; 2.04	1.82; 1.93; 2.08	1.89; 2.02

^{a,b} These assignments may be reversed; ^1H coupling constants (*J*, Hz), 1α : 10 β , 10; 1α : 2, 3; 2: 3, 11; 2: 4 β , 3; 3: 4 β , 3; 6 α : 6 β , 15; 6 β : 7 β , 3; 7 α : 7 β , 15; 7 β : 8 α , 3; 7 α : 8 α , 3; 11 α : 12 β , 12; 19: 19', 10. ^c Signal not identified.

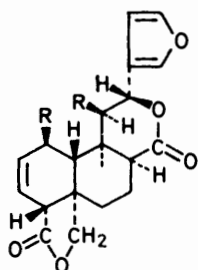
(2), $\text{C}_{24}\text{H}_{26}\text{O}_9$. Its structure forms the subject of this paper.

The nature of the oxygen functions was defined as follows. The ^{13}C n.m.r. spectrum (see Table) contained four ester type (O·CO) carbonyl signals (δ_{C} 169.1, 169.7, 170.0, and 174.4). The i.r. and ^1H n.m.r. spectra enabled these to be attributed to two acetoxy-groups [ν_{max} 1735br cm^{-1} , δ_{H} 1.98 and 2.05 (each 3 H, s)], a γ -lactone (ν_{max} 1775 cm^{-1}) and a δ -lactone (ν_{max} 1735 cm^{-1}). The remaining oxygen atom was present in a β -substituted furan ring (ν_{max} 870 cm^{-1} , δ_{H} 6.42, 7.42, and 7.51). The ^1H n.m.r. spectrum (see Table) contained a tertiary C–Me resonance (δ_{H} 1.07) together with an AB doublet (δ_{H} 4.16 and 4.35, *J* 10 Hz) which was assigned to a $\geq\text{C}\cdot\text{CH}_2\cdot\text{O}\cdot\text{C}(\text{O})$ group. The single frequency off-resonance decoupled ^{13}C n.m.r. spectrum (see Table) showed that the other carbon atoms bearing

resonances. In the light of the analytical data, splendidin was therefore a bicarbocyclic diterpenoid probably related to salviarin (1).

Reduction of splendidin with sodium borohydride gave an unstable lactol (3) which regenerated the parent δ -lactone on oxidation with chromium trioxide in pyridine. Acetylation of the lactol with acetic anhydride in pyridine, gave a stable acetate (4), $\text{C}_{26}\text{H}_{30}\text{O}_{10}$. The olefinic double bond in splendidin could be selectively hydrogenated over palladised charcoal to afford a dihydro-compound (5), $\text{C}_{24}\text{H}_{28}\text{O}_9$. Compared to splendidin, the dihydro-compound lacked one of the ^1H n.m.r. signals at δ 5.90 and a second signal at δ 5.73. These were therefore assigned to the olefinic protons. Another of the low-field CH–O signals (δ 5.51) had moved upfield to δ 5.21. This was therefore assigned to an allylic acetoxy CH–O. On the other hand the dihydro-

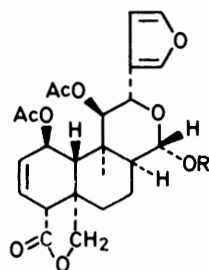
compound retained the doublets at δ 5.35 and 8.85 (J 12 Hz), which were therefore remote from the double bond.



(1) R = H

(2) R = OAc

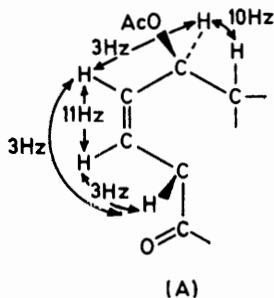
(5) R = OAc; 2,3-dihydro



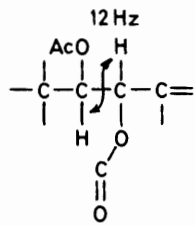
(3) R = H

(4) R = Ac

^1H Spin-decoupling studies performed at 220 MHz on splendidin and its transformation products enabled the functional groups to be related and lead to the part structures (A) and (B).



(A)



(B)

These fragments, together with the furan ring and the $\geq\text{C}-\text{CH}_2-\text{O}-\text{C}(\text{O})$ grouping, can be readily accommodated on the carbon skeleton of salviarin (1) which co-occurs with splendidin leading to the formulation (2). The magnitude of the 1H:10H and 11-H:12-H coupling constants enabled the stereochemistry of the acetoxy groups to be assigned whilst the size of the W allylic coupling between 2-H and 4-H signals can also be accounted for in this structure. The 8α -H stereochemistry is reflected in the magnitude (3 Hz) of the 7α -H: 8α -H and 7β -H: 8α -H coupling constants. An interesting feature of this stereochemistry is the *cis*-relationship between the 8-H and 9-Me; a similar relationship is found in columbin.² The absolute stereochemistry of these diterpenoids has yet to be determined.

EXPERIMENTAL

General experimental details have been described previously.³ 220 MHz N.m.r. spectra were determined on a Perkin-Elmer R 34 spectrometer through the courtesy of Dr. M. Barnard, Perkin-Elmer, Beaconsfield.

Isolation.—*Salvia splendens* (Labiatae) (ca. 2 kg) was obtained from the Botanic Gardens, University of Palermo, and extracted as described previously.¹ The extract was chromatographed on a dry silica column. Elution with 40% ethyl acetate–light petroleum gave splendidin (800 mg) which crystallized from aqueous methanol as needles, m.p. 236° , $[\alpha]_D^{20} -188^\circ$ (c 0.2) (Found: C, 62.7; H, 5.7. $\text{C}_{24}\text{H}_{26}\text{O}_9$ requires C, 62.9; H, 5.7%), ν_{max} 1775, 1735, 1248, and 870 cm^{-1} , m/e 458 (M^+) (3%), 398 (10), 356 (20), 204 (75), 189 (100), 176 (20), 143 (30), 135 (40), 110 (60), 95 (90), and 81 (100).

Reduction of Splendidin with Sodium Borohydride.—Splendidin (500 mg) in methanol (20 ml) was treated with sodium borohydride (500 mg) at room temperature. The lactol (3), m.p. 270° , crystallized immediately and was filtered off; ν_{max} 3300, 1750–1730, 1230, 1050, 1020, 960, 930, and 870 cm^{-1} ; $\delta(\text{C}_5\text{D}_5\text{N}; 90\text{ MHz})$ 1.08 (3 H, s), 1.88 (3 H, s), 2.01 (3 H, s), 3.08 (1 H, m), 3.14 (1 H, d, J 10 Hz) 4.20 and 4.53 (1 H each, d, J 10 Hz), 5.26 and 5.49 (1 H each, ABq, J 10 Hz), 5.64 (1 H, m), 5.78 (2 H, m), 6.08 (1 H, d, J 10 Hz), and 6.68, 7.37, and 7.47 (1 H each, br s). On standing, the compound decomposed. A portion was acetylated with acetic anhydride in pyridine to form the acetate (4) which crystallized from ethyl acetate–light petroleum as needles, m.p. 209 – 211° (Found: C, 62.2; H, 5.9. $\text{C}_{26}\text{H}_{30}\text{O}_{10}$ requires C, 62.1; H, 6.0%), ν_{max} 1770, 1740br, 1250, 1235, 1050, 1020, 965, and 872 cm^{-1} , m/e 442 ($M^+ - 60$), (3%), 400 (5), 383(7), 323 (18), 110 (100), 95 (40), 91 (30), and 81 (40).

Oxidation of the Lactol (3).—The lactol (3) (100 mg) in pyridine (5 ml) was treated with chromium trioxide (100 mg) overnight at room temperature. The solution was poured into ca. 0.1 N-hydrochloric acid and the product recovered in ethyl acetate to afford splendidin (55 mg), identical (m.p. and n.m.r.) to the natural product.

Catalytic Hydrogenation of Splendidin.—Splendidin (70 mg) in ethyl acetate (20 ml) was shaken in an atmosphere of hydrogen over 10% palladised charcoal (100 mg) until 1.1 mol of hydrogen was taken up. The solution was filtered and the solvent evaporated to afford dihydrosplendidin (5) which crystallized from ethyl acetate–light petroleum as needles, m.p. 270° (Found: C, 62.6; H, 6.0. $\text{C}_{24}\text{H}_{28}\text{O}_9$ requires C, 62.6; H, 6.1%), ν_{max} 1750–1730, 1230, 1020, 965, and 870 cm^{-1} , m/e 400 ($M^+ - 60$) (15%), 358 (25), 340 (10), 325 (10), 202 (75), 189 (100), 176 (20), 161 (35), 131 (40), 110 (60), 95 (100), 91 (95), and 81 (100).

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