

## **<sup>13</sup>C Nuclear Magnetic Resonance Spectral Analysis of Santalin and Santarubin Permethyl Ethers**

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The complete <sup>13</sup>C n.m.r. spectral analysis of the condensed biflavonoids per-*O*-methyl-santarubin and -santalin is reported.

SANTALINS and santarubins are the red colouring matters of the heartwoods of some Asian and African *Pterocarpus* species (*e.g.* sandalwood and camwood). They are fused biflavonoids, and their complex structures have been fully elucidated only recently.<sup>1,2</sup> Individual santalins and santarubins are different methyl ethers of the same parent phenols, methylation of which gives one or other of the corresponding two permethyl ethers. In view of the complex structures of these compounds, of recent interest in <sup>13</sup>C n.m.r.

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spectra of flavanoids,<sup>3</sup> and of the potential utility of such data in biogenetic studies we report here the <sup>13</sup>C n.m.r. spectral analysis of both per-*O*-methyl-santarubin (1) and -santalin (2).

### EXPERIMENTAL

The spectra were measured for solutions in CDCl<sub>3</sub> with a Varian XL-100-15 spectrometer. The chemical shifts,

<sup>1</sup> A. Arnone, L. Camarda, L. Merlini, and G. Nasini, *J.C.S. Perkin I*, 1975, 186.

<sup>2</sup> A. Arnone, L. Camarda, L. Merlini, G. Nasini, and D. A. H. Taylor, preceding paper.

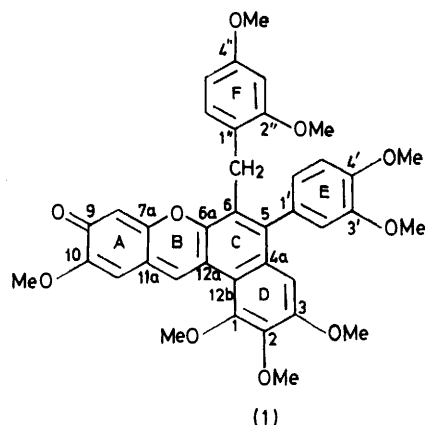
<sup>3</sup> A. Pelter, R. S. Ward, and T. I. Gray, *J.C.S. Perkin I*, 1976, 2475, and references quoted therein.

given in p.p.m. relative to internal  $\text{Me}_4\text{Si}$  are accurate to within  $\pm 0.1$  Hz for protons, and C-H coupling constant values are accurate to within  $\pm 1$  Hz. Concentrations of  $150 \text{ mg ml}^{-1}$  were used for  $^{13}\text{C}$  signal assignments. The assignments of carbon signals were made from 'gated' undecoupled spectra, by use of  $^1\text{H}$  noise decoupling,  $^1\text{H}$  single-frequency off-centre decoupling (SFOCD), and single-frequency selective heteronuclear decoupling (SFSD).

#### DISCUSSION

In this paper a full utilization of  $^{13}\text{C}$ - $^1\text{H}$  coupling patterns has been made; hitherto such data have rarely been used for complicated molecules. In complex cases it is difficult to use the additive effect of the substituents, especially in polyaromatic compounds with *ortho*-substituents.

All the long-range couplings fall in the ranges already reported. In particular, the values of the *meta*-coupling constants ( $^3J$ ) are between 5.0 and 9.0 Hz, the two *peri*-coupling constants which could be measured [ $^3J(\text{C-12}, \text{H-11})$  4.5;  $^3J(\text{C-5}, \text{H-4})$  3.0 Hz] have values similar to those in acetoxynaphthalenes,<sup>4</sup> and values of  $^3J$  between carbon and hydrogen nuclei on different rings [e.g.  $^3J(\text{C-5}, \text{H-2}')$ ] are *ca.* 3.0 Hz. Among the *ortho*-coupling constants, the larger (3.0–3.5 Hz) all belong to carbon nuclei bearing an oxygen atom. Values of  $^2J$  for the bridging methylene carbon atom fall between 5.5



and 6.0 Hz, whereas  $^3J$  is 4.0–5.0 Hz.<sup>5</sup> Couplings between  $\text{C}\cdot\text{O}\cdot\text{CH}_3$  and  $\text{C}\cdot\text{O}\cdot\text{CH}_3$  are in the range 3.0–4.0 Hz.

**Santarubin Permethylether (1).**—The signal at lowest field (178.4 p.p.m.) was easily assigned to the carbonyl carbon (C-9), and that at 29.3 p.p.m. to the methylene carbon.

**Aromatic CH.** These assignments were straightforward, as the aromatic proton region in the  $^1\text{H}$  n.m.r. spectrum was resolved sufficiently to allow a complete analysis of this region; therefore the corresponding carbon signals could be identified by SFSD (Table 1). However, carbon atoms of rings E and F, except for C-5'', could also be assigned independently by analysis of the

undecoupled spectrum and by comparison with data for the model compounds 1,2- (3) and 1,3-dimethoxybenzene (4).

**Aromatic quaternary carbons.** The eleven signals between 159.0 and 143.7 p.p.m. were expected to be the ten quaternary carbon nuclei bearing oxygen atoms and one aromatic carbon nucleus not bearing oxygen (C-5; see later). Signals for C-7a and -6a (156.7 and 149.8 p.p.m.) were identified by their loss of *meta*-coupling with H-12 on selective irradiation at the frequency of this proton, giving a doublet of doublets and a triplet, respectively, whereas on irradiation at 4.0 p.p.m. the C-6a signal only loses the three-bond coupling with the  $\text{CH}_2$  group (Table 1). The remaining nine carbon signals were all decoupled by systematic irradiation within the narrow (3.6–4.1 p.p.m.) region which includes all the OMe and the  $\text{CH}_2$  signals, and gave six broad and three sharp signals. The latter were assigned to C-1, -3, and -2 (respectively at 150.7, 152.0, and 143.7 p.p.m.) because C-1 (singlet) is the sole carbon atom bearing OMe with no proton in either a three- or a two-bond relationship, and the C-2 and -3 signals become sharp doublets as they retain only the interaction with H-4. In fact, upon irradiation at the frequency of H-4 all three carbon nuclei gave quartets due to coupling with their own OMe groups. The assignment of C-3 *vs.* C-2 is based on the high field position of the latter, consistent with the value for C-2 in 1,2,3-trimethoxybenzene,<sup>6</sup> and on the values of the coupling constants with H-4. The 8.0 Hz splitting for C-2 indicates *meta*-coupling, whereas the 3.0 splitting of C-3 is consistent with a two-bond (*ortho*) interaction.

Comparison with the model compounds (3) and (4) allowed us to assign with reasonable certainty the two pairs of signals at 159.0 and 157.7 p.p.m. and at 148.7 and 148.5 p.p.m. to C-2'' and -4'' and to C-3' and -4', respectively. The individual signals were then identified on the basis of the following observations. The signal at 159.0 is broader ( $W_{\frac{1}{2}}$  24 Hz) than that at 157.7 p.p.m. (19 Hz) but on irradiation at  $\delta$  3.6–4.0 they become similar. Therefore the former must be coupled with the methylene signal (*cf.* toluene<sup>5</sup>) as expected only for C-2''. The C-3' and C-4' signals were distinguished by irradiation of the same region: they gave respectively a broad doublet (*meta*-coupling with H-5') and a broad triplet (*meta*-coupling with H-2' and -6'). The broadening of the signals must be due to *ortho*-couplings, which, however, are not large enough to be measured accurately.

The signal at 154.9 p.p.m. was assigned to the last oxygenated carbon nucleus (C-10) because on irradiation at  $\delta$  3.6–4.0 it gave a doublet of doublets [ $^3J(\text{C-10}, \text{H-8})$  6.0;  $^2J(\text{C-10}, \text{H-11})$  3.0 Hz]. Moreover, the chemical shift was the same as in the spectrum of santalin permethyl ether, where it could be easily identified by the

<sup>5</sup> M. Hansen and H. J. Jakobsen, *J. Magnetic Resonance*, 1975, **20**, 520.

<sup>6</sup> E. Wenkert, H. E. Gottlieb, O. R. Gottlieb, M. O. Da S. Pereira, and M. D. Formiga, *Phytochemistry*, 1976, **15**, 1547.

<sup>4</sup> P. Granger and M. Maugras, *J. Magnetic Resonance*, 1976, **22**, 405.

strong shift induced by co-ordination of  $\text{Eu}(\text{dpm})_3$  to the nearby carbonyl group.

The remaining signal of this group (144.9 p.p.m.) was attributed to C-5; upon irradiation at  $\delta$  4.0 ( $\text{CH}_2$ ) it gave a quartet ( $J$  3.0 Hz) due to the remaining couplings with H-4, -6', and -2'. Under the same conditions, C-6 and -1'' gave a singlet and a triplet ( $J$  6.0 Hz), the latter due to three-bond coupling with H-3'' and H-5''.

Moreover, irradiation of the aromatic region also made visible for C-1'' and C-5 the triplet structure due to coupling with the  $\text{CH}_2$  group. The C-11a and -12b signals were located at 121.6 and 117.5 p.p.m.; they have three-bond couplings with H-8 and -4, respectively. Both these signals can be distinguished from that of C-1' since the latter is not decoupled (130.4 p.p.m.) upon irradiation at the frequency of H-12. The sharpening

TABLE I  
Chemical shifts and coupling constants \*

Santarubin permethyl ether (1)			Santalol permethyl ether (2)		
$\delta_{\text{H}}$	$J/\text{Hz}$	$\delta_{\text{C}}$	Carbon	$\delta_{\text{C}}$	$J/\text{Hz}$
	$^3J(\text{C-1, OMe-1})$ 3.5	150.7 (q)	C-1	150.7 (q)	<i>b</i>
	$^3J(\text{C-2, OMe-2})$ 4.0	143.7 (dq)	C-2	143.6 (dq)	<i>b</i>
	$^3J(\text{C-2, H-4})$ 8.0				
	$^3J(\text{C-3, Ome-3})$ 4.0	152.0 (dq)	C-3	152.1 (dq)	<i>b</i>
	$^2J(\text{C-3, H-4})$ 3.0				
6.80	<i>a</i>	104.6	C-4	104.1 (d)	$^1J(\text{C-4, H-4})$ 161.0
	$^2J(\text{C-4a, H-4}) \leq 1$	128.3 (s)	C-4a	128.4 (s)	
	$^3J(\text{C-5, H-4})$ 3.0	144.9 (dddt)	C-5	141.1 (ddt)	$^3J(\text{C-5, H-4})$ 3.0
	$^3J(\text{C-5, H-2'})$ 3.0				$^3J(\text{C-5, H-6'})$ 3.0
	$^3J(\text{C-5, H-6'})$ 3.0				$^3J(\text{C-5, CH}_2)$ 4.5
	$^3J(\text{C-5, CH}_2)$ 5.0				
	$^2J(\text{C-6, CH}_2)$ 6.0	127.1 (t)	C-6	128.1 (t)	<i>b</i>
	$^3J(\text{C-6a, H-12})$ 6.0	149.8 (dt)	C-6a	149.6 (dt)	<i>b</i>
	$^3J(\text{C-6a, CH}_2)$ 4.5				
	$^2J(\text{C-7a, H-8})$ 3.5	156.7 (ddd)	C-7a	156.5 (ddd)	<i>b</i>
	$^3J(\text{C-7a, H-11})$ 9.0				
	$^3J(\text{C-7a, H-12})$ 6.5				
6.36	<i>a</i>	103.9	C-8	103.6 (d)	$^1J(\text{C-8, H-8})$ 164.0
	$^3J(\text{C-9, H-11})$ 7.0	178.4 (d)	C-9	178.4 (d)	<i>b</i>
	$^2J(\text{C-10, H-11})$ 3.0	154.9 (ddq)	C-10	155.1 (ddq)	<i>b</i>
	$^3J(\text{C-10, H-8})$ 6.0				
	$^3J(\text{C-10, OMe-10})$ 3.0				
6.72	<i>a</i>	104.0	C-11	103.9 (dd)	$^1J(\text{C-11, H-11})$ 162
	$^3J(\text{C-11a, H-8})$ 5.5	121.6 (d)	C-11a	121.6 (d)	$^3J(\text{C-11, H-12})$ 5
	$^2J(\text{C-11a, H-12}) \leq 1$				<i>b</i>
9.58	$^1J(\text{C-12, H-12})$ 168.0	134.5 (dd)	C-12	134.1 (dd)	<i>b</i>
	$^3J(\text{C-12, H-11})$ 4.5				
	$^2J(\text{C-12a, H-12}) \leq 1$	114.3 (s)	C-12a	114.5 (s)	<i>b</i>
	$^3J(\text{C-12b, H-4})$ 7.0	117.5 (dd)	C-12b	117.5 (dd)	<i>b</i>
	$^3J(\text{C-12b, H-12})$ 3.0				
	$^3J(\text{C-1', H-5'})$ 7.5	130.4 (d)	C-1'	119.0 (dd)	$^3J(\text{C-1', H-3'})$ 6.5
6.67	$^1J(\text{C-2', H-2'})$ 158.0	112.7 (dd)	C-2'	161.3br (s)	$^3J(\text{C-1', H-5'})$ 6.5
	$^3J(\text{C-2', H-6'})$ 7.0			(158.0)	$W_{\frac{1}{2}}$ 20
	$^3J(\text{C-3', H-5'})$ 7.0	148.7 (m)	C-3'	98.9 (dd)	$^1J(\text{C-3', H-3'})$ 158.0
					$^3J(\text{C-3', H-5'})$ 5.0
	$^3J(\text{C-4', H-2'})$ 7.0	148.5 (m)	C-4'	161.3br (s)	$W_{\frac{2}{3}}$ 20
	$^3J(\text{C-4', H-6'})$ 7.0			(158.0)	
6.99	$^1J(\text{C-5', H-5'})$ 160.0	111.1 (d)	C-5'	104.9 (dd)	$^1J(\text{C-5', H-5'})$ 162.5
6.82	$^1J(\text{C-6', H-6'})$ 163.0	121.7 (dd)	C-6'	132.0 (d)	$^3J(\text{C-5', H-3'})$ 5.0
	$^3J(\text{C-6', H-2'})$ 7.0				$^1J(\text{C-6', H-6'})$ 160.0
	$^3J(\text{C-1'', H-3''})$ 6.0	120.9 (ddt)	C-1''	132.5br (s)	$W_{\frac{2}{3}}$ 17
	$^3J(\text{C-1'', H-5''})$ 6.0				
	$^2J(\text{C-1'', CH}_2)$ 5.5				
	$^3J(\text{C-2'', H-6''})$ 9.0	159.0 (m)	C-2''	112.1br (d)	$^1J(\text{C-2'', H-2''})$ 157
	$W_{\frac{1}{2}}$ 24				$W_{\frac{2}{3}}$ of each line 14
6.41	$^1J(\text{C-3'', H-3''})$ 160	98.0 (dd)	C-3''	148.5br (s)	$W_{\frac{1}{2}}$ 17
	$^3J(\text{C-3'', H-5''})$ 6.0				
	$^3J(\text{C-4'', H-6''})$ 9.0	157.7br (d)	C-4''	147.2br (s)	$W_{\frac{2}{3}}$ 23
	$W_{\frac{1}{2}}$ 19				
6.23	<i>a</i>	103.9	C-5''	111.1 (d)	$^1J(\text{C-5'', H-5''})$ 157.0
6.56	$^1J(\text{C-6'', H-6''})$ 158	128.5 (dt)	C-6''	120.7 (ddt)	$^1J(\text{C-6'', H-6''})$ 160
	$^3J(\text{C-6'', CH}_2)$ 4.0				$^3J(\text{C-6'', H-2''})$ 7.0
					$^3J(\text{C-6'', CH}_2)$ 4.0
	$^1J(\text{CH}_2)$ 129	29.3 (t)	$\text{CH}_2$	33.7 (t)	$^1J(\text{CH}_2)$ 129
	$^1J(\text{OMe})$ 144	61.2 (q)	OMe-1	61.2 (q)	$^1J(\text{OMe})$ 144
	$^1J(\text{OMe})$ 144	60.9 (q)	OMe-2	60.7 (q)	$^1J(\text{OMe})$ 144
		55.2—55.9	6 OMe	55.5—55.7	

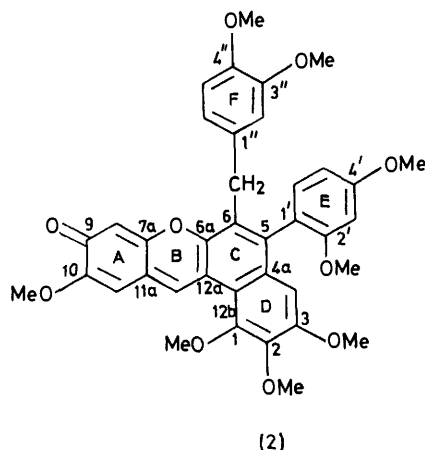
\* Spectra measured in  $\text{CDCl}_3$  (conc. 150 mg  $\text{ml}^{-1}$ ).

<sup>b</sup> Not detected owing to overlapping of signals. <sup>b</sup> Identical with data for (1).

of the signals at 128.3 and 114.3 p.p.m. upon irradiation at the frequencies of H-4 and H-12 respectively, due to the vanishing of the small two-bond interactions ( ${}^2J \leq 1$  Hz), is selective enough to allow their assignment to C-4a and -12a.

*Santalin Permethyl Ether* (2).—The signal at 178.4 p.p.m. was readily assigned to the carbonyl group (C-9) and that at 33.7 to the  $\text{CH}_2$ .

*Aromatic CH.* Most of the aromatic proton signals were superimposed in the  ${}^1\text{H}$  spectrum; thus no  ${}^1\text{H}$



analysis was possible, and extensive use of SFSD was not possible. Therefore we had to rely on comparison with suitable models and with santarubin permethyl ether. Irradiation at the frequency of H-12, which gives a separate signal at low field ( $\delta$  9.58) in the  ${}^1\text{H}$  spectrum, allowed the assignment of the C-12 (134.1) and C-11 (103.9 p.p.m.) signals: the former signal loses the one-bond and the latter the three-bond coupling with this proton. From the analysis of the undecoupled spectrum and by comparison with the models (3) and (4) we assigned the signals at 120.7, 112.1, and 111.1 p.p.m. to C-6'', -2'', and -5'' and those at 132.0, 104.9, and 98.9 p.p.m. to C-6', -5', and -3', respectively. The preferred complexation of  $\text{Eu}(\text{dpm})_3$  with the carbonyl group allowed us to distinguish the C-8 from the C-4 signal; C-8, being  $\beta$  to the carbonyl oxygen, suffers a strong upfield shift.<sup>7</sup>

*Aromatic quaternary carbons.* As expected, C-7a, -6a, -1, -3, -2, and -10 showed chemical shifts, patterns, and behaviour upon irradiation very similar to those of the corresponding carbons of santarubin permethyl ether when the H-12 frequency and the  $\delta$  3.6–4.1 region (including the  $\text{CH}_2$  and all the OMe signals) were irradiated. These signals were thus assigned on the basis of the same reasoning as used for compound (1). The C-4' and -2' (161.3 and 158.0 p.p.m.) and C-3'' and -4'' (148.5 and 147.2 p.p.m.) signals were assigned by comparison with compounds (3), (4), and (1). Although the former two could not be differentiated, C-4'' showed a half-width ( $W_{1/2}$  23 Hz) larger than that of C-3'' (17 Hz) and consistent with two three-bond couplings, allowing their respective assignment.

The C-6, -5, and -1'' signals (128.1, 141.1, and 132.5 p.p.m.), on decoupling from the methylene, gave respectively a singlet, a doublet of doublets (two  ${}^3J$  of 3.0 Hz with both H-4 and -6'), and a broad signal. The chemical shift of the last (C-1'') was in agreement with that of the corresponding carbon in the model 3,4-dimethoxytoluene (5). Inspection of the undecoupled spectrum allowed the assignment of C-1' (dd, two  ${}^3J$  of 6.5 Hz) and of the remaining nuclei C-11a, -12b, -4a, and -12a. For this latter group, the chemical shifts, shapes of the signals in the undecoupled spectrum, and decoupling results were very similar to those of the corresponding carbon nuclei in (1).

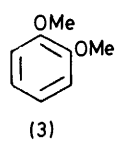
TABLE 2

Lanthanoid-induced shifts for santalin permethyl ether (2)

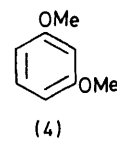
Ring	$\delta_{\text{C}}$	$\Delta\delta$		
		${}^{13}\text{C}$	${}^1\text{H}$	
OMe-2	D	61.2	3.5	2.8
OMe-1	D	60.7	1.6	1.5
OMe-3	D		1.3 or	0.9
			1.5	
OMe-10	A		17.2 or	9.3
			17.0	
OMe-3''	F	55.7 or	9.2 or	4.2 <sup>a</sup>
		55.5	9.0	
OMe-4''	F		9.2 or	4.1 <sup>a</sup>
			9.0	
OMe-2'	E		0.9 or	0.7
			0.7	
OMe-4'	E		0.4	0.2

<sup>a</sup> May be interchanged.

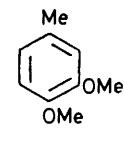
*Methoxy-groups.* The signals of the OMe groups could not be assigned because most of them (except two) are superimposed. However, on addition of  $\text{Eu}(\text{dpm})_3$  some separation was achieved. Table 2 gives the



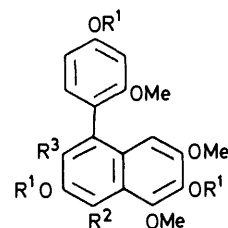
(3)



(4)



(5)



- (6) a,  $\text{R}^1 = \text{H}$ ,  $\text{R}^2 = \text{H}$ ,  $\text{R}^3 = \text{CHO}$   
 b,  $\text{R}^1 = \text{Ac}$ ,  $\text{R}^2 = \text{H}$ ,  $\text{R}^3 = \text{CHO}$   
 c,  $\text{R}^1 = \text{Me}$ ,  $\text{R}^2 = \text{H}$ ,  $\text{R}^3 = \text{CHO}$   
 b,  $\text{R}^1 = \text{Me}$ ,  $\text{R}^2 = \text{CHO}$ ,  $\text{R}^3 = 3,4\text{-(OMe)}_2\text{C}_6\text{H}_3\cdot\text{CH}_2$

induced shifts for  ${}^{13}\text{C}$  and  ${}^1\text{H}$  spectra at an equimolar ratio of compound (2) and the shift reagent. The OMe

<sup>7</sup> M. Hirayama, E. Edagawa, and Y. Hanyu, *J.C.S. Chem. Comm.*, 1972, 1345.

signals in the  $^1\text{H}$  spectrum have been assigned previously on the basis of induced shifts,<sup>2</sup> and the strong similarity in behaviour of carbon and hydrogen signals under the same conditions makes the assignment of the carbon shifts reliable. Moreover, OMe-1 and OMe-3 could be distinguished by selective heteronuclear irradiation of the  $^1\text{H}$  signals, which are 0.4 p.p.m. apart. Table 2 shows that two OMe carbon nuclei (OMe-1 and OMe-2) resonate at lower field than the others in the spectrum of (2). The assignment is confirmed by comparison with 1,2,3-trimethoxybenzene<sup>6</sup> for OMe-2 and with the models (6a—d) for OMe-1. In fact, whereas in 1-methoxynaphthalene OMe-1 appears at 55.2 p.p.m., in compounds (6a—c) it undergoes a shift to lower field of

ca. 5—6 p.p.m. [60.8 for (6a), 61.9 for (6b), 61.0 or 61.2 p.p.m. for (6c)]: in this latter compound, as well as in (6d) (60.3 or 61.1 p.p.m.) OMe-2 also appears in this range, whereas all the other OMe carbons appear at between 55.4 and 55.9 p.p.m. The downfield effect can be attributed to spatial interaction with both H-12 in (2) or the formyl group in (6d) and the adjacent OMe-2.<sup>8</sup> This is in agreement with the strong nuclear Overhauser effect (17%) shown by the *peri*-hydrogen atom upon irradiation of OMe-1 in compound (6b).

[7/640 Received, 14th April, 1977]

<sup>8</sup> K. S. Dhami and J. B. Stothers, *Canad. J. Chem.*, 1966, **44**, 2855.