Polymeric Proanthocyanidins. ^{13}C N.M.R. Studies of Procyanidins

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^{13}C N.m.r. chemical shifts have been assigned to 40 natural and synthetic proanthocyanidins, related flavan-3-ols, and their peracetate derivatives. These data may be used to draw structural inferences from the related spectra of proanthocyanidin polymers.

PROANTHOCYANIDIN polymers have been shown to consist entirely of flavan-3-ol units by a combination of techniques including ^{13}C n.m.r. spectroscopy.[1] The ^{13}C n.m.r. spectra of the polymers and related molecules are now considered in more detail. Prior to this study ^{13}C n.m.r. data has been published of procyanidins [2,3] and related flavan-3-ols,[4] and has been used to deduce the stereochemistry and configuration of procyanidin dimers.[5,6]

The current study presents a comprehensive range of proanthocyanidin structures, with special emphasis on those possessing units with a 2,3-*cis*-configuration.[1] This unit has the advantage that the spectra of the oligomeric phenols are free of the effects of conformational isomerism at 30 °C.[6] Spectra of the proanthocyanidin monomers, oligomers and polymers have been run under identical conditions of solvent [$^2H_6$]-acetone–water, 1 : 1 v/v] and temperature (30 °C). This enables direct comparison between the oligomer and polymer spectra. Benzyl sulphides were run in dry [$^2H_6$]acetone for solubility reasons. All peracetate spectra were run in deuteriochloroform.

Model Compounds.—The spectra of the simple flavan-3-ols, (1)—(13), may be assigned in detail (Table 1). The quaternary carbons attached to oxygen in the A-ring cannot be distinguished from one another however. The A-ring C–O carbon signals are in the region 154—159 p.p.m. and those of the B-ring with a pyrocatechol substitution pattern near 145 p.p.m.

The C-6 and C-8 A-ring carbons of (+)-catechin (1) and (−)-epicatechin (2) were assigned from the spectra of the model compounds (8), (9), (11), and (12). The position of the *o*-hydroxybenzyl substituent has been unequivocally established for these compounds,[7] and C-8 is observed to be more shielded than C-6. This is similar to the assignments for the mono-*o*-hydroxybenzyl derivatives of pinocembrin, where C-8 was also observed to be more shielded.[8]

The assignments for C-6 and C-8 are supported by T_1 measurements on (+)-catechin (1) and (−)-epicatechin (2). The observed values for C-6 and C-8 are 0.23 s and 0.30 s for (+)-catechin (1) and 0.21 s and 0.29 s for (−)-epicatchin (2) respectively. These fit closely theoretical values of T_1 for these compounds calculated using known molecular co-ordinates,[9] and considering them to behave as ellipsoids in solution. This work is reported in detail elsewhere.[10]

The C-3″ and C-5″ signals of compounds (3)—(6) may be readily distinguished from C-6 and C-8. In the 2,3-*cis*-compounds, (5) and (6), the appending phloroglucinol is rotating freely [6] and appears as a two-carbon singlet, whereas C-6 and C-8 show the expected *meta–meta* coupling in the proton-coupled spectrum. The n.m.r. spectra of 2,3-*trans*-isomers, (3) and (4), display rotational isomerism at room temperature,[6] the coalescence temperature being approached at 30 °C. Therefore, C-3″ and C-5″ are distinguished from C-6 and C-8 as broadened signals with about twice the line width of the other signals in the spectrum.

The C-4 and C-α signals of 4-benzylthioepicatechin (7) were differentiated by the latter appearing as a triplet in the proton coupled spectrum. The chemical shift of C-α is similar to that observed in peptide benzylthio-derivatives (38 p.p.m.).[11]

The pyrocatechol B-ring signals were assigned by consideration of the proton-coupled spectrum.

The chemical shifts for (−)-epicatechin (2) are similar to those previously reported.[2-4]

The ^{13}C chemical shifts of the heterocyclic ring carbons of the compounds (3) and (5) in $(CD_3)_2SO$ have previously been reported.[6] The γ-shielding effect of a pseudoaxial phenyl substituent at C-4 on C-2 was used to diagnose stereochemistry.[6] The pseudoaxial substituent also has shielding effects on the A-ring through the π-electron system; the C-6 and C-8 resonances are shifted upfield 0.7—1.3 p.p.m. in (5) and (6), compared with (3) and (4), and the C-4a resonance is shifted upfield 5.8 p.p.m.

Introduction of a pseudoaxial benzylthio group at C-4 compound (7), produces a 14.3 p.p.m. downfield shift, much less than the shift of 42 p.p.m. produced by a hydroxy-group.[6]

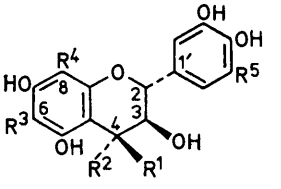
Procyanidin Spectra.—The spectra of dimers and trimers possessing procyanidin units with a 2,3-*cis*-stereochemistry are given in Table 2. Only those chemical shifts with structural significance are included. The B-ring resonances are over-lapping and often complex, but generally the chemical shifts are those predicted from the simpler monomers, Table 1, (1)—(13).

The C-6 and C-8 resonances of the upper units of the dimers and trimers are readily distinguished from the lower units by the possession of *meta–meta* coupling by the former resonances in the proton-coupled spectrum. The assignments in the dimers (14)—(21) are unequi-

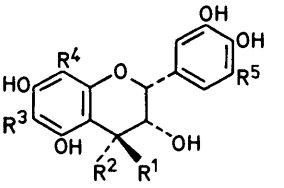
vocal since their configurations have been independently established.[6] It may be noted in the pairs of isomeric procyanidins B1/B7 (14, 17) and B2/B5 (15, 16) that the higher field position of the C-8 resonances is maintained by both the substituted and unsubstituted C-6 and C-8 resonances. This is predicted from the spectra of *o*-hydroxy-benzyl substituted (+)-catechin [Table 1, (8)—(10)] and (−)-epicatechin [Table 1, (11)—(13)]. established independently. However, unequivocal assignments cannot be made for all the resonances in Table 2 for these compounds. Many of the resonances are readily assigned, such as the heterocyclic ring carbons of the lower catechin or epicatechin unit, and the C-6 and C-8 resonances of the upper procyanidin unit.[12] The remainder were assigned by analogy with the spectral shifts of the dimers (14)—(17) and model

TABLE 1

^{13}C N.m.r. chemical shifts of monomeric flavan-3-ols



(1),(3),(4),(8),(9),(10)



(2),(5),(6),(7),(11),(12),(13)

(1) $R^1 = R^2 = R^3 = R^4 = R^5 = H$
(2) $R^1 = R^2 = R^3 = R^4 = R^5 = H$
(3) $R^1 = R^3 = R^4 = R^5 = H$; $R^2 = C_6H_2(OH)_3$-2,4,6
(4) $R^1 = R^3 = R^4 = H$; $R^2 = C_6H_2(OH)_3$-2,4,6; $R^5 = OH$
(5) $R^1 = C_6H_2(OH)_3$-2,4,6; $R^2 = R^3 = R^4 = R^5 = H$
(6) $R^1 = C_6H_2(OH)_3$-2,4,6; $R^2 = R^3 = R^4 = H$; $R^5 = OH$
(7) $R^1 = SCH_2Ph$; $R^2 = R^3 = R^4 = R^5 = H$
(8) $R^1 = R^2 = R^4 = R^5 = H$; $R^3 = CH_2C_6H_4OH$-*o*
(9) $R^1 = R^2 = R^3 = R^5 = H$; $R^4 = CH_2C_6H_4OH$-*o*
(10) $R^1 = R^2 = R^5 = H$; $R^3 = R^4 = CH_2C_6H_4OH$-*o*
(11) $R^1 = R^2 = R^4 = R^5 = H$; $R^3 = CH_2C_6H_4OH$-*o*
(12) $R^1 = R^2 = R^3 = R^5 = H$; $R^4 = CH_2C_6H_4OH$-*o*
(13) $R^1 = R^2 = R^5 = H$; $R^3 = R^4 = CH_2C_6H_4OH$-*o*

Compound	2	3	4	4a	6	8	1′	2′	3′	4′	5′	6′	
(+)-Catechin (1)	82.0	67.9	28.1	100.9	96.7	95.7	131.5	115.6	145.4	145.5	116.6	120.3	
(−)-Epicatechin (2)	79.1	66.8	28.6	100.3	96.8	96.0	131.8	115.4	145.0	145.2	116.4	119.6	
Catechin-(4α→2)-phloroglucinol (3)	83.7	72.9	37.9	106.8	97.6	96.4	131.7	116.3	145.3	145.7	116.5	121.0	95.8, 97.0 [a]
Gallocatechin-(4α→2)-phloroglucinol (4)	83.8	73.0	37.9	107.0	97.8	96.4	131.1	108.7	146.2	133.9	146.2	108.7	95.9 97.1 [a]
Epicatechin-(4β→2)-phoroglucinol (5)	76.6	72.6	36.5	102.0	96.5	95.7	132.2	115.5	144.9	145.2	116.4	119.6	96.5 [a]
Epigallocatechin-(4β→2)-phoroglucinol (6)	76.6	72.5	36.4	102.2	96.5	95.7	131.7	107.3	146.2	133.0	146.2	107.3	96.5 [a]
4-Benzylthioepicatechin (7)	74.4	70.3	42.9	99.4	96.4	95.2	131.0	114.8	144.4	144.4	115.7	118.8	36.9 [b]
6-(*o*-Hydroxybenzyl)catechin (8)	82.0	68.2	29.0	101.5	108.8	96.3	131.6	116.0	145.5	145.5	116.5	120.5	23.6 [c]
8-(*o*-Hydroxybenzyl)catechin (9)	82.4	68.2	29.0	101.5	96.7	106.9	131.7	116.0	145.5	145.6	116.5	120.5	23.7 [c]
6,8-Di-(*o*-hydroxybenzyl)catechin (10)	82.4	68.5	29.7	102.4	109.6	108.4	131.7	115.9	145.6	145.7	116.4	120.6	24.0 [c]
6-(*o*-Hydroxybenzyl)epicatechin (11)	78.9	66.9	29.1	100.8	108.8	96.6	131.8	115.4	145.0	145.1	116.4	119.6	23.6 [c]
8-(*o*-Hydroxybenzyl)epicatechin (12)	79.2	66.6	28.9	100.6	96.8	107.2	132.0	115.4	145.0	145.2	116.4	119.6	23.6 [c]
6,8-Di-(*o*-hydroxybenzyl)epicatechin (13)	79.5	66.8	29.8	101.0	108.8	108.0	132.2	115.3	145.3	145.5	115.7	119.4	23.8, 24.0 [c]

[a] C-3″, C-5″ of phloroglucinol ring. [b] Methylene attached to sulphur. [c] Methylene on *o*-hydroxybenzyl function.

Here the chemical-shift difference between the substituted C-6 and C-8 signals is 1.9 p.p.m., larger than the difference between the unsubstituted carbon resonances, 0.6 p.p.m. The spectra of compounds (1), (2), (8), (9), (11) and (12), and of the dimers (14)—(17) show that there is generally a downfield shift of 0.5—1.0 p.p.m. in the signal of the unsubstituted carbon on benzylation at C-6 or C-8. This is extended to doubly benzylated (+)-catechin (10) and (−)-epicatechin (13).

Consideration of the chemical shift of C-4 for the pairs of linkage isomers in Table 2 [*i.e.* (14) and (16); (15) and (17) *etc*] shows that it consistently occupies a less shielded position (0.3—0.4 p.p.m.) in the C(4)–C(6) linked isomer. Similarly the spectra of the 4-phloroglucinol substituted flavan-3-ols, (3)—(6), show that C-4 is more shielded (1.4—1.5 p.p.m.) in the 2,3-*cis*- than the 2,3-*trans*-isomer.

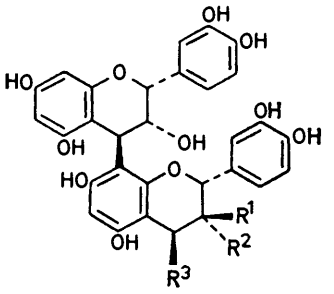
The structures of the trimers (22)—(25) have been compound (5). The higher field C-3 resonance in (22) and (23), and also in the model compound (20), was assigned to the middle flavan-3-ol unit, since models show that this carbon is in a highly shielded position compared with the dimers.

In contrast, the assignments are reversed in (24) as the top and middle units are C(4)–C(6) linked, producing a much less hindered structure, and the position of the C-3 resonance of the upper unit would be expected to be similar to that of procyanidin B5 (16).

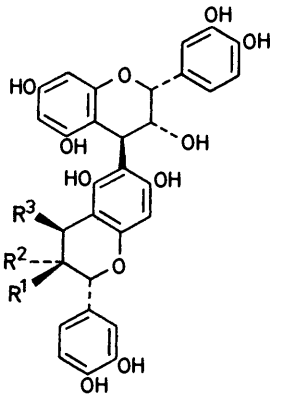
Polymer Spectra.—Two examples of procyanidin polymers containing all 2,3-*cis*-units are also given in Table 2. The *Vicia sativa* polymer possesses a catechin terminal unit, as shown by the C-2 resonance at 81.3 p.p.m., whereas the terminal C-2 unit signal of the *Chaenomeles chinensis* polymer is at 78.9 p.p.m. and is, therefore, consistent with an epicatechin terminal unit. These have been confirmed by degradation.[1]

TABLE 2

^{13}C N.m.r. shifts of 2,3-*cis*-procyanidins



(14),(15),(18),(20),(22),(23),(25)



(16),(17),(19),(21),(24)

(14) procyanidin B1; $R^2 = R^3 = H$; $R^1 = OH$
(15) procyanidin B2; $R^1 = R^3 = H$; $R^2 = OH$
(16) procyanidin B5; $R^1 = R^3 = H$; $R^2 = OH$
(17) procyanidin B7; $R^2 = R^3 = H$; $R^1 = OH$
(18) $R^1 = H$; $R^2 = OH$; $R^3 = SCH_2Ph$
(19) $R^1 = H$; $R^2 = OH$; $R^3 = SCH_2Ph$
(20) $R^1 = H$; $R^2 = OH$; $R^3 = C_6H_2(OH)_3$-2,4,6
(21) $R^1 = H$; $R^2 = OH$; $R^3 = C_6H_2(OH)_3$-2,4,6
(22) $R^1 = H$; $R^2 = OH$; R^3 = 8-(+)-catechin
(23) $R^1 = H$; $R^2 = OH$; R^3 = 6-(+)-catechin
(24) $R^1 = H$; $R^2 = OH$; R^3 = 8-(+)-catechin
(25) $R^1 = H$; $R^2 = OH$; R^3 = 8-(−)-epicatechin

Compd.	Unit *	2	3	4	6	8	
Procyanidin B1 (14)	T	76.4	72.6	36.6	96.1	95.6	
	B	81.7	67.8	28.0	97.0	108.1	
Procyanidin B2 (15)	T	76.6	72.8	36.7	96.5	96.0	
	B	79.1	66.2	29.1	97.4	107.7	
Procyanidin B5 (16)	T	76.6	72.1	37.0	96.9	96.0	
	B	78.9	66.6	28.9	108.6	96.9	
Procyanidin B7 (17)	T	76.7	72.0	37.0	96.4	95.9	
	B	82.0	67.9	28.7	108.4	96.7	
4″-Benzylthioprocyanidin B2 (18)	T	76.9	72.8	36.8	96.4	96.0	
	B	75.4	70.5	43.8	97.6	107.1	37.3 [a]
4″-Benzylthioprocyanidin B5 (19)	T	77.0	72.3	37.1	96.5	96.0	
	B	75.1	71.1	43.8	108.3	96.6	37.1 [a]
Epicatechin-(4β→8)-epicatechin-(4β→2)-phloroglucinol (20)	T	76.5	73.0	36.8	96.5	96.1	
	B	76.5	71.6	36.8	97.2	107.6	96.5 [b]
Epicatechin-(4β→6)-epicatechin-(4β→2)-phloroglucinol (21)	T	76.6	72.5	37.2	96.5	96.1	96.2 [b]
	B	76.9	72.5	37.0	107.3	96.9	
Epicatechin-(4β→8)-epicatechin-(4β→8)-catechin (22)	T	76.7	72.9	36.9	96.6	96.1	
	M	76.9	71.7	36.9	97.2	106.9	
	B	81.4	67.5	28.2	97.2	108.0	
Epicatechin-(4β→8)-epicatechin-(4β→6)-catechin (23)	T	76.6	73.1	36.9	96.4	96.1	
	M	76.6	71.2	37.3	97.5	107.4	
	B	82.0	68.0	28.9	108.5	96.5	
Epicatechin-(4β→6)-epicatechin-(4β→8)-catechin (24)	T	76.8	72.0	37.1	96.8	96.1	
	M	76.4	72.5	36.9	107.1	96.4	
	B	81.5	67.9	28.3	96.8	107.1	
Epicatechin-(4β→8)-epicatechin-(4β→8)-epicatechin (25)	T	76.5	73.0	36.8	96.4	96.0	
	M	76.5	71.9	36.8	97.1	107.1	
	B	78.9	66.2	29.2	97.5	107.6	
Vicia sativa (leaf)	T	76.6	72.4	37.1	97.5 [c]	107.4	
	B	81.3	67.4				
Chaenomeles (fruit)	T	76.6	73.0, 72.4	37.2	97.5 [c]	107.5	
	B	78.9	66.2				

* T = top, B = bottom, M = middle.

[a] Methylene on benzylthio-group. [b] Unsubstituted carbons on appending phloroglucinol ring. [c] The maximum of this signal is assigned to C-6 on the basis that most interflavanoid links are C(4)–C(8). The signal will contain a C-8 component, however.

The unsubstituted C-6/C-8 signals of the polymers are centred on 97.5 p.p.m. The spectra of the trimers (22)—(26) show that this is consistent with the chemical shift for C(4)–C(8) linked 2,3-*cis*-units, and the relative intensity of this signal shows that the majority of linkages in the polymers must be of this configuration. However, the signal at 97.5 p.p.m. is not symmetrical, and fine structure is evident in the upfield portion of the signal. The fine structure is only partly resolved at 20 MHz and further studies are being undertaken at higher fields.

The C-2 signal of 2,3-*cis*-polymers is much narrower

than that of the C-3 signal. For instance, in the *Vicia sativa* spectrum the linewidth at half height ($W_{\frac{1}{2}}$) for C-2 is 26 Hz, whereas that for C-3 is 42 Hz. Consideration of the trimer spectra shows that the broadening of the C-3 signal is due to linkage isomerism. The range of chemical shifts of C-3 in the trimers (22)—(24) is these shifts is particularly useful in this field since the peracetate derivatives of proanthocyanidins may be easily prepared in high yield and are simply purified. In contrast the phenols or their methyl ethers are acid labile and more difficult to purify.

The assignment of the ^{13}C n.m.r. spectra of the mono-

TABLE 3

^{13}C N.m.r. chemical shifts of flavan-3-ol peracetates

Compound		Chemical shifts (p.p.m.) [h]												
		2	3	4	4a	6	8	8a	1′	2′	3′	4′	5′	6′
(+)-Catechin (1)		77.8	68.4	24.0	110.2	108.8	107.7	154.5	136.2	121.8	142.2	142.2	123.7	124.4
(−)-Epicatechin (2)		76.7	66.7	26.1	109.7	108.8	108.0	155.0	135.9	122.1	142.0	142.1	123.2	124.4
4-Benzylthioepicatechin [a] (7)		72.6	70.3	38.2	108.7	109.8	107.8	155.2	135.8	122.2	142.0	142.1	123.2	124.5
Epicatechin-(4β→2)-phloroglucinol [b,e] (5)		73.5	70.8	33.9	110.5	108.8	107.7	155.0	135.8	122.2	142.0	142.0	123.2	124.6
Epigallocatechin-(4α→2)-phloroglucinol [c,f] (6)		73.8	70.7	33.8	110.5	108.9	107.7	154.8	135.5	119.2	143.3	136.6	143.3	119.2
Gallocatechin-(4→)-phloroglucinol [d,g] (4)		79.3	71.6	36.8	114.9	110.4	108.7	155.6	134.3	119.9	143.3	135.2	143.3	119.9
6-(*o*-Hydroxybenzyl)catechin (8)		77.9	68.5	24.6	111.6	117.6	109.1	152.9	136.1	121.8	142.0	142.1	123.7	124.6
8-(*o*-Hydroxybenzyl)catechin (9)		77.7	68.2	24.0	110.3	109.3	117.4	152.6	136.0	121.6	142.0	142.0	123.5	124.2
6,8-Di-(*o*-hydroxybenzyl)catechin (10)		77.8	68.4	24.8	111.7	117.9	118.5	151.3	135.9	121.8	140.9	142.1	123.5	124.4
Dimers														
Procyanidin B1 (14)	Top	73.6	70.9, 70.6	34.1, 34.5		108.6, 108.8	107.2, 107.8							
	Bottom	78.3	68.4, 68.1	27.1		110.7	117.1							
Procyanidin B2 (15)	Top	73.7	71.7	34.1		108.7	107.3							
	Bottom	77.3	66.8	26.7		110.4	116.8							
Procyanidin B5 (16)	Top	73.7	70.9	34.5		108.7	107.5							
	Bottom	76.6	66.3	26.4		116.5, 117.0	110.7, 111.7							
Procyanidin B7 (17)	Top	73.9	71.1	34.0, 34.3		108.7, 109.7	107.6							
	Bottom	77.8	68.4, 68.2	24.5		116.6, 117.1	110.5, 111.6							
4″-Benzylthioprocyanidin B2 [i] (18)	Top	77.8, 74.4	71.1, 70.9	34.1, 34.3		108.9	107.2, 108.1							
	Bottom	73.4, 72.8	70.6, 70.3	39.0, 38.8		111.4, 111.9	116.3, 117.1							
4″-Benzylthioprocyanidin B5 [i] (19)	Top	73.9	70.8, 71.5	33.7		108.7, 108.3	107.5							
	Bottom	72.4	69.5	38.4		117.4, 117.5	110.0, 111.5							

[a] Methylene on sulphur is at 36.2 p.p.m. [b] C-3″, C-5″ are at 114.5 and 115.4 p.p.m. respectively. [c] C-3″, C-5″ are at 114.4 and 115.4 p.p.m. respectively. [d] C-3″, C-5″ are at 113.5 and 114.8 p.p.m. respectively. [e] C-1″ 120.7 p.p.m. [f] C-1″ 121.3 p.p.m. [g] Methylene on sulphur 36.3 p.p.m. [h] Where there are two chemical shifts given, the first is for the major conformational isomer.

1.9 p.p.m. (38 Hz) and that of C-2 is only 0.4 p.p.m. The chemical-shift range of the C-3 signals is, therefore, similar to the $W_{\frac{1}{2}}$ value of the C-3 signal of the *Vicia sativa* tannin spectrum. This is also supported by dynamic n.m.r. measurements which show that T_1 and η are very similar for the C-2 and C-3 signals of polymer spectra, and hence peak broadening must be due to chemical-shift dispersion.[10]

We have also observed that $W_{\frac{1}{2}}$ varies for the C-3 signal of polymers containing entirely 2,3-*cis*-units. For instance $W_{\frac{1}{2}}$ for the *Vicia sativa* and *Chaenomeles chinensis* polymers is 42 and 41 Hz respectively, whereas it is 53 Hz for the *Photinia glabrescens* polymer. This implies that the latter is likely to possess a higher degree of configurational isomerism than the former polymers.

Acetate Spectra.—The ^{13}C n.m.r. chemical shifts for the peracetate derivatives of a number of the compounds in Tables 1 and 2 are given in Table 3. A knowledge of meric flavan-3-ol peracetates is straightforward, and all resonances except C-5 and C-7 may be unequivocally assigned. The chemical shift of C-8a is now readily distinguishable from C-5 and C-7, as the electron-withdrawing effect of the acetate function causes an upfield shift of the latter resonances of *ca.* 7 p.p.m., whereas the C-8a resonance is almost unaffected.

The bulky acetate groups cause the spectra of the peracetates of both the phloroglucinol addition compounds and the dimers to display the effects of conformational isomerism.[6] The C-3″ and C-5″ resonances of the phloroglucinol derivatives are readily distinguished from C-6 and C-8 because of the downfield position of the former resonance due to the triacetate functionality of the appending phloroglucinol ring.

The ^{13}C n.m.r. spectra of the dimeric procyanidin peracetates are complex. Conformational isomerism causes pairing of many of the ^{13}C n.m.r. signals.[6] Whether or not two signals are observed depends on the

relative degree of shielding in the averaged environment of each conformational isomer. The population of each conformational isomer is normally unequal, so that the ^{13}C n.m.r. signals appear as pairs with unequal intensities. In some of the spectra the signal for the minor rotational isomer is small.

The spectra of the peracetates are generally less useful than those of the corresponding phenols for structural diagnostic purposes. The chemical shifts are less sensitive to the effects of configurational isomerism, apart from the useful exception of the C-2 signal of the lower flavan-3-ol unit of the B-dimers. The C-2 resonance is the same as in (+)-catechin (1) and (−)-epicatechin (2) for the C(4)–C(6) linked dimers, B7 (17) and B5 (16) respectively, whereas it is shifted *ca.* 0.5—0.7 p.p.m. downfield in the C(4)–C(8) linked dimers, B1 (14) and B2 (15) respectively.

Conclusion.—The ^{13}C n.m.r. spectra of phenolic flavan-3-ols have chemical shifts which are characteristic of most of their key structural features including heterocyclic ring stereochemistry and A- and B-ring substitution patterns. The spectra of the simple mono- and oligomeric flavan-3-ols are likely to provide the key to the structure of polymeric proanthocyanidins through high-field n.m.r. studies.

EXPERIMENTAL

Spectra were determined at 20 MHz on a Varian FT-80A spectrometer in [$^2H_6$]acetone–water (1 : 1, v/v) for phenols, or $CDCl_3$ for peracetates, using $SiMe_4$ as reference, at 30 °C. Spectral widths were generally 5 000 Hz. Chemical shifts were measured relative to internal $SiMe_4$ (for peracetates), or relative to external $SiMe_4$, with correction for the solvent magnetic susceptibility (for phenols).

Compounds (1)—(7) and (14)—(25) are all natural products, or derived from natural products, as discussed elsewhere.[1,2,6,13] The *o*-hydroxybenzyl derivatives of (+)-catechin and (−)-epicatechin were synthesized by the condensation of *o*-hydroxybenzyl alcohol with flavan-3-ols in mild acid solution.[7]

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