Condensed Tannins: Base-Catalysed Reactions of Polymeric Procyanidins with Toluene-α-thiol. Lability of the Interflavanoid Bond and Pyran Ring.

Peter E. Laks*† and Richard W. Hemingway
Southern Forest Experiment Station, USDA-Forest Service, 2500 Shreveport Highway, Pineville, LA 71360

Reaction of polymeric procyanidins (condensed tannins) with toluene-α-thiol at pH 12.0 and 23 °C gave predominantly one stereoisomer of 1,3-bisbenzylthio-1-(3,4-dihydroxyphenyl)-3-(2,4,6-trihydroxyphenyl)propan-2-ol (**10**) by stereoselective reaction at C-4 and C-2 of the quinone methide derived from the upper 2,3-*cis* procyanidin units. Smaller amounts of two isomers of 1-benzylthio-1-(3,4-dihydroxyphenyl)-3-(2,4,6-trihydroxyphenyl)propan-2-ol (**4**) were obtained by reaction at the C-2 of catechin obtained from the terminal units. At higher temperatures, (**10**) loses toluene-α-thiol preferentially from C-1 to give 1-benzylthio-1-(3,4-dihydroxyphenyl)-3-(2,4,6-trihydroxyphenyl)-propan-2-one (**11**) by a tautomeric rearrangement of the quinone methide *via* an enol to the ketone. Loss of toluene-α-thiol from (**4**) gave 1-(3,4-dihydroxyphenyl)-3-(2,4,6-trihydroxyphenyl)propan-2-one (**5**) by a similar rearrangement. This compound further rearranges to 1-(3,4-dihydroxyphenyl)-4,6-dihydroxyindan-2-one (**6**).

Condensed tannins are often extracted and/or allowed to react at alkaline pH in the course of manufacture of specialty polymers such as tannin-based adhesives. With the exception of some reactions of monomeric flavan-3-ols,[1–4] and a few flavan derivatives with good leaving groups at C-4,[5,6] little work has been published on the base-catalysed reactions of these compounds. When (+)-catechin (**2**) is dissolved in alkaline solutions under comparatively mild conditions (*i.e.* pH 10.5 and ambient temperature), cleavage within the pyran ring gives a quinone methide (**3**) that recondenses with the phloroglucinol hydroxy group to give both (+)-catechin (**2**) and (+)-epicatechin (**12**) in the relative proportions of *ca.* 3.5 to 1.[1–3] At higher pH and/or temperature, the quinone methide [(**3**) Scheme 1] undergoes intramolecular condensation by nucleophilic attack of the phloroglucinol A ring on the quinone methide with subsequent rearrangement to catechinic acid, an enolic form of 6-(3,4-dihydroxyphenyl)-7-hydroxybicyclo-[3.3.1]nonane-2,4,9-trione (**13**).[1,4] Similar intramolecular condensations and rearrangements have been proposed in the reactions of condensed tannins in alkaline solution, but no evidence, other than observations of a reduction of phloroglucinol functionality in reactions with aldehydes and appearance of strong carbonyl absorption in the i.r. region,[7] has been offered for this conclusion.

In contrast to the reaction of flavan-3-ol (*i.e.* (+)-catechin], derivatives with good leaving groups at C-4 (*i.e.* thio (**14**) or hydroxy (**15**) functions] at pH 9.0 and ambient temperature give the quinone methides (**16**) or (**17**) without cleavage of the pyran ring.[5] This reaction has been used for the synthesis of epicatechin-(4β→8)-catechin, epicatechin-(4β→6)-epicatechin, and the 'branched' trimer epicatechin-(4β→8)-catechin-(6→4β)-epicatechin.[5,6] These results prompted questions about the reactions of polymeric procyanidins in solutions at higher pH, particularly, as to the relative labilities of the interflavanoid bond and the ether linkage in the pyran ring.

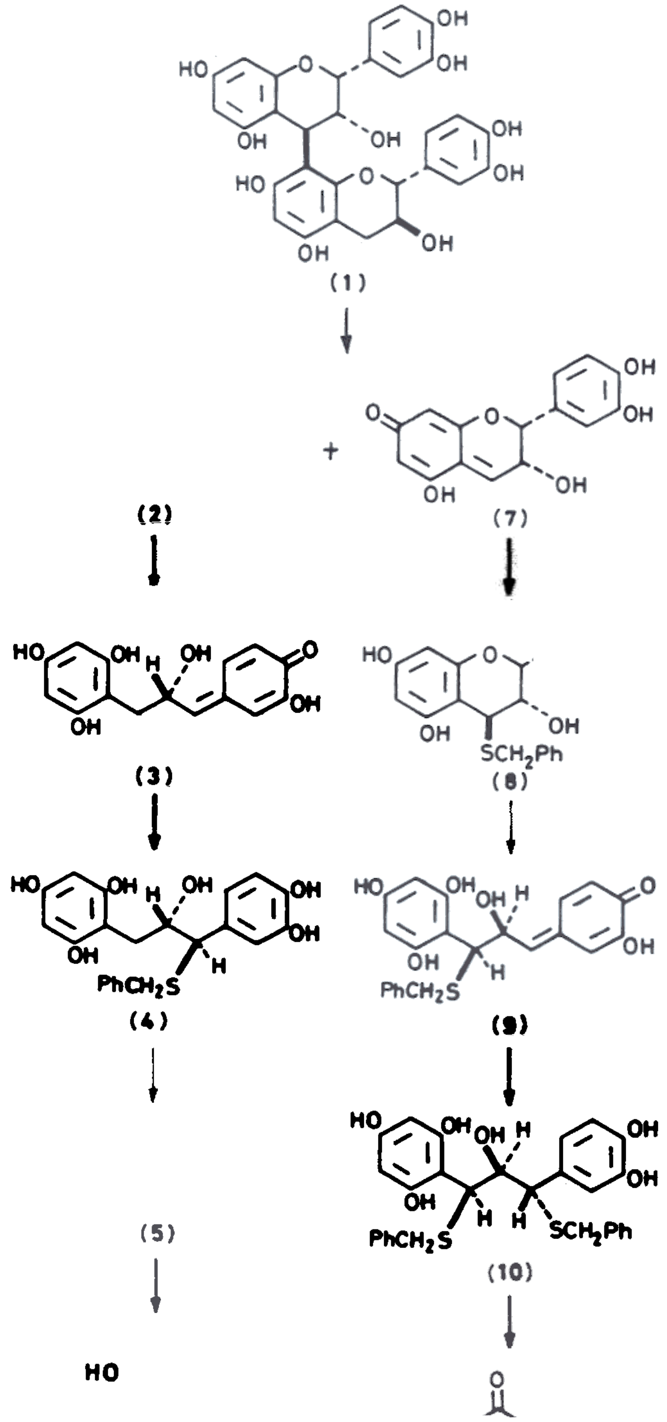
The polymers studied were obtained from the bark of loblolly pine trees (*Pinus taeda* L.).[8] Oligomeric procyanidins isolated from the bark [the dimers epicatechin-(4β→8)-catechin (**1**), epicatechin-(4β→6)-catechin and small amounts of catechin-(4α→8)-catechin[9] as well as the trimers epicatechin-(4β→8)-epicatechin-(4β→8)-catechin, epicatechin-(4β→6)-epicatechin-(4β→8)-catechin, and epicatechin-(4β→8)-epicatechin-(4β→6)-catechin[10]] reflect the structure of the higher polymers as revealed by ^{13}C n.m.r.[8,11,12] and thiolytic degradation products.[8–10] The (4β→6) and (4β→8) interflavanoid bonds are present in the relative proportions of *ca.* 3 to 1, respectively. These tannins have a number average molecular weight of 2 500 to 3 000 (*ca.* 9 flavanoid units) and dispersivity ranging from 2 to 4.[8,13] To simplify Scheme 1, the polymers are represented by the dimer (**1**).

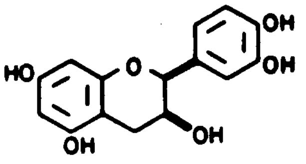
Reaction of loblolly pine bark tannins with toluene-α-thiol at pH 12.0 and ambient temperature for 16 or 48 h produced a series of diarylpropan-2-ol derivatives (Scheme 1). One of the compounds isolated was 1-benzylthio-1-(3,4-dihydroxyphenyl)-3-(2,4,6-trihydroxyphenyl)propan-2-ol (**4**). Fast atom bombardment mass spectroscopy (f.a.b.–m.s.) of (**4**) showed an $M + 1$ signal of 415 in the positive ion spectrum, in agreement with the calculated molecular weight of 414. ^{13}C N.m.r. spectrometry indicated that this compound was a mixture of two stereoisomers in a ratio of *ca.* 2:3 (isomeric at the C-1 of the propyl function). The chemical shifts of the carbon atoms in the two isomers are similar, with the largest difference of 0.9 Hz for the asymmetric C-1. The differences in the chemical shift of analogous carbon atoms in the two isomers decrease with distance from the asymmetric centre. The ^{13}C n.m.r. spectrum of the major isomer showed equivalent phloroglucinol tertiary carbons at a chemical shift of 96.8, the propyl C-3 at 30.4, the propyl alcohol at 76.9, and the disubstituted, asymmetric C-1 at 56.9 p.p.m. The presence of one benzylthio group on each isomer was evident from the PhCH_2S signals at 36.8 and 36.6 p.p.m.[12] The same isomers in a similar ratio were obtained from the reaction of (+)-catechin with toluene-α-thiol at pH 12.0 and ambient temperature.

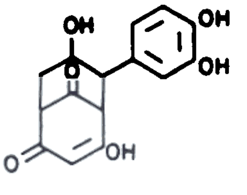
The ^{1}H n.m.r. spectrum of (**4**) in $CDCl_3$—$(CD_3)_2CO$ was complex owing both to the presence of two stereoisomers and the asymmetry of the molecule which made the gem protons at C-3 and PhCH_2S non-equivalent. The gem protons on these carbons have coupling constants of 15 and 13.5 Hz. The presence of two stereoisomers was evident from a doubling of some proton signals with consistently different signal intensities. A signal at δ 7.2 (s, br) arose from the phenyl protons of the two isomers, while the signals from the pyrocatechol rings overlapped to give a complex set of signals in the range 6.5—7.0. The

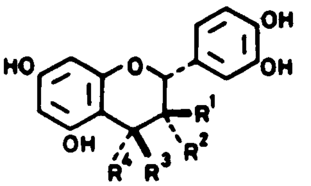
---

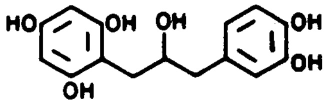
† *Current Address:* Institute of Wood Research, Michigan Technological University, Houghton, MI 49931




(12)


(13)


(14) $R^1 = H$, $R^2 = OH$, $R^3 = SCH_2Ph$, $R^4 = H$
(15) $R^1 = OH$, $R^2 = H$, $R^3 = H$, $R^4 = OH$

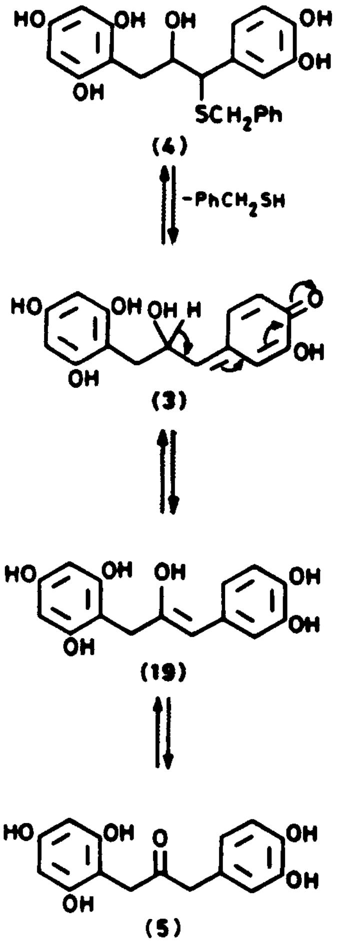

(18)

protons on the hydroxylated C-2 positions of the two isomers were also unresolved and gave a complex multiplet centred at δ 4.0. The major isomer gave a sharp singlet at δ 5.95 due to the two equivalent protons on the phloroglucinol ring, a doublet at δ 3.69 (J 8 Hz, 3-H), and two quadruplets centred at 2.92 and 2.56 (J_{AB} 2.5, 6.5 Hz, 2 × 1-H). The minor isomer resulted in a similar set of signals at δ 6.0, 3.65 (J 7 Hz), 3.14 (J 2 Hz), and 2.46 (J 7.5 Hz). In both cases, the gem coupling constant of the protons on C-3 was 15.0 Hz. The signals due to PhCH_2S in the two isomers had the same chemical shift which resulted in a single double doublet with signals at 3.61 and $\overline{3.46}$, and a coupling constant of 13.5 Hz. The inner signals were much more intense than the outer ones owing to the small difference in chemical shift and large coupling constant. The measured ratios of outer to inner line intensities is 0.074 which agrees well with the calculated, theoretical value of 0.071.

The formation of two stereoisomers in nonequivalent amounts is consistent with the intermediate of this reaction being a quinone methide in an extended conformation as shown by structure (3). Previous work on the reactions of flavan derivatives with good leaving groups at C-4 indicated facile formation of quinone methide intermediates under mild alkaline conditions,[5,6] a conclusion supported by the spectral studies of Attwood *et al.*[14] Analogous formation of a quinone methide (3) in cleavage of the pyran ring is clearly consistent with the rapid epimerization of flavan-3-ols in mild alkaline solutions.[1,2] In this case, nucleophilic attack by the toluene-α-thiol would occur preferentially at the least hindered side, away from the C-2 hydroxy group, and implying that the isomer occurring in higher concentration is the 1*R* isomer as shown in structure (4).

Reaction of (4) with Raney nickel gave 1-(3,4-dihydroxyphenyl)-3-(2,4,6-trihydroxyphenyl)propan-2-ol (18). This compound has been reported previously, but without a complete description of its n.m.r. spectra.[15] The ^{13}C n.m.r. spectrum showed the signal due to the symmetrical phloroglucinol carbons at 96.9, the propyl C-3 at 31.6, the hydroxylated C-2 at 75.8, and the C-1 methylene at 44.[illegible] p.p.m. Apart from the latter signal and absence of a phenylmethane group, this spectrum was very similar to that of the previous compound discussed (4).

The ^1H n.m.r. of this compound was again quite complex



Scheme 2. Elimination and tautomerisation of the catechin–toluene-α-thiol adduct to a propanone derivative

owing to the asymmetric nature of C-2 which made the gem protons on C-1 and C-3 non-equivalent. The spectrum has essentially four sets of signals—a multiplet at 6.7 due to the tertiary protons on the pyrocatechol ring, a sharp singlet at δ 5.95 from the phloroglucinol tertiary hydrogens, a multiplet at δ 4.05 for the proton on C-2, and a complex set of signals centred on δ 2.75 due to the protons on C-1 and C-3. The signal at 4.05 can be interpreted as a single proton being split by four adjacent, non-equivalent hydrogens with coupling constants of 2.5, 4.5, 5.0, and 9.0 Hz. The multiplet at 2.75 can be interpreted as four overlapping double-doublets centred at chemical shifts of 2.57 (*J* 8, 14 Hz), 2.67 (*J* 5, 9 Hz), 2.83 (*J* 5, 9 Hz), and 2.99 (*J* 3, 14 Hz).

A second product isolated from the reaction of loblolly pine bark tannins with toluene-α-thiol at pH 12.0 and 23 °C for 16 h, was the 1,3-bisbenzylthio derivative (**10**). High resolution f.a.b.–m.s. showed $M + 1 = 537.1393$, in agreement with the calculated value for $C_{29}H_{28}O_6S_2 + 1$ of 537.1406. Several isomers of this compound were evident from the multiplicity of signals in the ^{13}C n.m.r. spectrum. However, in contrast to the formation of (**4**), one isomer was preferentially produced in a relative yield of *ca.* 90% of the product. The major isomer was isolated by column chromatography. Substitution at both C-1 and C-3 of the propyl function was evident from resonances at δ 48.6 and 55.0 p.p.m., respectively, with the propyl C-2 at δ 79.2 p.p.m. Equivalent phloroglucinol tertiary carbons appeared at δ 96.7 p.p.m. PhCH_2S signals at δ 36.4 and 37.3 p.p.m. were consistent with the presence of two benzylthio groups. Reduction of (**10**) with Raney nickel also gave a stereoisomer of the diarylpropanol, (**18**).

In acetone solution, the ^1H n.m.r. spectrum showed a complex multiplet at δ 7.1 due to the phenyl rings, a further multiplet in the range 6.8—6.2 for the pyrocatechol ring protons, a sharp singlet at 5.9 from the phloroglucinol ring, a 1 H doublet at 4.65 (*J* 4 Hz), a 1 H double doublet at 4.4 (*J* 4, 9 Hz), a further doublet at δ 3.6 (*J* 9 Hz), a 2 H double doublet resulting from two mutual splitting of the gem hydrogens at δ 3.65 and 3.38 (*J* 11.5 Hz), and a 2 H singlet at δ 3.52.

The stereoselective formation of predominantly one isomer implies that interflavanoid bond cleavage occurs first, followed by opening of the pyran ring. In acid-catalysed cleavage of 2,3-*cis*-procyanidins, thiol addition proceeds through the quinone methide intermediate (**7**), giving the 3,4-*trans* isomer (**8**) exclusively. Although (**8**) was not isolated from the alkaline reactions of procyanidins with toluene-α-thiol, the equivalent adduct was observed in similar reactions with phloroglucinol as the nucleophile.[16] This implies a 1*S* configuration for (**10**). When the pyran ring opens to form the quinone methide intermediate (**9**), the 1-benzylthio group and the 2-hydroxy become *cis*. The bulky 1-benzylthio group in (**10**) makes *trans* addition to C-3 more predominant than in the formation of (**4**). On the basis of the mechanism, the major product should be 1*S*,3*S* as shown in structure (**10**).

Since the 1-benzylthio substituent (α to the phloroglucinol ring) would be expected to be a good leaving group, the stereochemistry of the final products should reflect thermodynamic rather than kinetic control; in contrast the 3-benzylthio substituent would not be expected to be a good leaving group.[17,18] Dreiding models show that substitution at C-1 after loss of toluene-α-thiol from (**10**) can be expected to be stereoselective, predominantly *cis* to the aliphatic hydroxy group and *trans* to the 3-benzylthio substituent on the basis of less steric hindrance. The stereochemistry of (**10**) as shown in Scheme 1 is, therefore, consistent with that expected from thermodynamic control.

The products (**4**) and (**10**) are unstable in alkaline solution and after 48 h at 23 °C or 12 h at 100 °C, three products were isolated that initially gave a red colour fading to an intense purple or blue, when sprayed with vanillin–HCl on cellulose t.l.c. plates. Separations on Sephadex LH-20 gave pure isolates of these compounds. One was identified as 1-(3,4-dihydroxyphenyl)-3-(2,4,6-trihydroxyphenyl)propan-2-one (**5**). The calculated molecular weight of 290 was confirmed by a positive-ion f.m.b.–m.s. showing a very strong $M + 1$ signal at 291. The presence of a carbonyl group was confirmed by f.t.–i.r. spectroscopy which showed a strong absorbance at 1 732 cm^{-1} and by ^{13}C n.m.r. spectroscopy where a signal at δ 212.1 p.p.m. was observed. Equivalent tertiary phloroglucinol carbons were observed at a chemical shift of 96.3 p.p.m., while the propyl C-3 and C-1 were apparent at 38.1 and 48.7 p.p.m. The rest of the carbon spectrum showed typical pyrocatechol B ring and quaternary phloroglucinol A ring absorbances.

The ^1H n.m.r. of this compound was comparatively simple, showing the pyrocatechol ring absorbances in the range 6.3—6.8, a sharp singlet for the phloroglucinol ring protons at 6.0, and two, 2 H singlets at 3.60 and 3.64 p.p.m. The latter signals were assigned to the methylene groups on either side of the carbonyl.

The second compound that gave a purple reaction with vanillin–HCl is a benzylthio derivative of the previously discussed compound (**11**). The ^{13}C n.m.r. spectrum was similar to that of (**5**) except for the addition of absorbances due to a benzylthio function at δ 36.2 and *ca.* 130 p.p.m., and shift of the signal from the propane carbon α to pyrocatechol to δ 58.2. The positive ion f.a.b.—m.s. showed a clear $M + 1$ signal at 413.

in agreement with the calculated molecular weight of 412. The ^1H n.m.r. spectrum of **(11)** was again quite simple. The phenyl group resulted in a singlet at δ 7.2, the pyrocatechol ring signals being apparent in the range 6.5—7.0, the phloroglucinol protons gave a sharp singlet at 5.95, a 1 H singlet at δ 4.75 was due to 3-H, while 1-H and $PhCH_2S$ gave 2 H singlets at 3.65 and 3.55 p.p.m., respectively.

The third compound isolated from the extended reaction of tannins with alkaline toluene-α-thiol gave a light blue colour with vanillin–HCl, in contrast to the dark purple of the last described two compounds. This compound was identified as 1-(3,4-dihydroxyphenyl)-4,6-dihydroxyindan-2-one **(6)**. An f.t.—i.r. spectrum showed strong carbonyl absorbance at 1 732 cm^{-1}, while the ^{13}C [$(CD_3)_2SO$] n.m.r. spectrum had a typical carbonyl signal at δ 214.7 p.p.m. Other important resonances in the carbon spectrum were the two hydroxylated quaternary resorcinolic carbons at δ 157.8 and 154.2, the tertiary resorcinol carbons at δ 103.1 and 101.6, the tertiary C-1 of the cyclopentane ring at δ 58.8, and 3-methylene at δ 40.6 p.p.m. F.a.b.—m.s. analysis of this compound was done in both the positive ion and negative ion modes. The former showed a $M + 1$ signal at 273, while the latter showed a $M - 1$ signal at 271. Both results agree with the calculated molecular weight of 272. High-resolution f.a.b.—m.s. indicated a molecular weight of 273.0765, in close agreement with the calculated figure of 273.0763.

The ^1H n.m.r. spectrum of **(6)** showed absorption typical of pyrocatechol rings plus two signals from the hydrogens on the resorcinol ring at δ 6.1 and 6.35 (J 2 Hz). 1-H produced a 1 H singlet at 4.37, while 3-CH_2 gave a 2 H singlet at δ 3.38. No conclusions could be drawn concerning the stereochemistry at C-1 from this data.

The reactions of polymeric procyanidins with toluene-α-thiol at pH 12.0 and ambient temperature are summarized in Scheme 1. Both the interflavanoid bond and the heterocyclic ring undergo ready cleavage with the formation of quinone methides which react with the nucleophilic thiol to produce benzylthio derivatives of diarylpropanoids. Catechin cleaved from the terminal unit forms two 1-benzylthio isomers **(4)** from attack on the heterocyclic ring. Formation of predominantly one stereoisomer of **(10)** from the 2,3-*cis* chain extender units suggests that the interflavanoid bond cleavage occurs first. This would restrict substitution at C-4 to one isomer, *trans* to the 3-hydroxy group, as occurs in acid-catalysed reactions of 2,3-*cis* procyanidins with thiols. Small amounts of epicatechin-(4β)-phloroglucinol were isolated from a similar alkaline reaction of tannins with phloroglucinol.[16] The equivalent benzylthio derivative **(10)** is also initially formed in this case. Subsequent substitution of the quinone methide produced from cleavage of the pyran ring is then stereoselective.

Much larger amounts of **(10)** were obtained from reactions for 16 h than for 48 h at 23 °C. Low yields of **(10)** were obtained from reactions at 100 °C for 12 h. The highest yields of **(10)** were obtained from the most mild reaction conditions studied and was equivalent to *ca.* 25% molar yield per C_{15} unit. The rapid formation of **(10)** at ambient temperature indicates that the interflavanoid bond is far more labile to cleavage at pH 12.0 than in acetic acid solutions.[19]

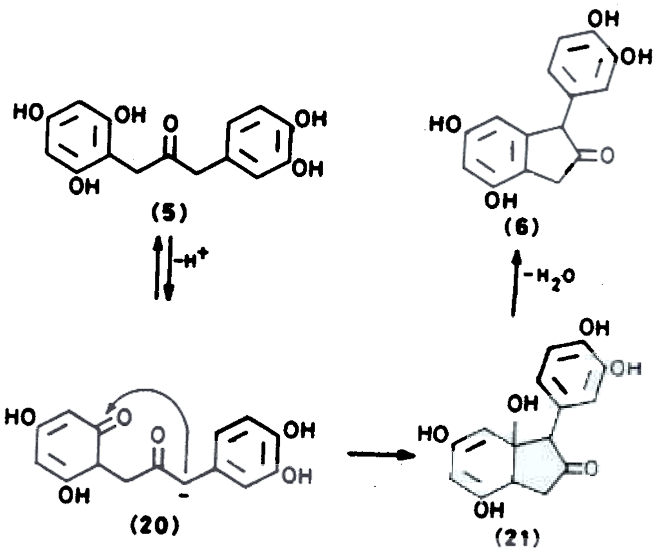
The propanone compounds **(5)** and **(11)** can be formed from quinone methide intermediates by tautomeric shifts of protons. The diarylpropanone **(5)** is formed by a tautomeric shift of the quinone methide [(3), Scheme 2] to form initially an enol **(19)** which then rearranges to the ketone **(5)**. The formation of **(11)** would proceed in a similar manner from the bisbenzylthio adduct **(10)**, except by a quinone methide formed through the phloroglucinol ring. The fact that the concentration of these compounds increases with time, while the thiol adducts disappear, infers that these reactions are in equilibria as shown.

Table 1. Selected ^{13}C n.m.r. chemical shifts for diarylpropane derivatives from reaction of condensed tannins with toluene-α-thiol at pH 12.0

	Carbon number				
	Propane			A-Ring	
Compd.	3	2	1	3	5
(4)[a]	56.9	76.9	30.4	96.8	96.8
(10)[a,b]	55.0	79.2	48.6	96.7	96.7
(18)[a,b]	44.2	75.8	31.6	96.9	96.9
(5)[a]	48.7	212.1	38.1	96.3	96.3
(11)[c]	58.2	206.0	36.4	95.0	95.0
(6)[c,d]	58.8	214.7	40.6	101.6 (C-5)	103.1 (C-7)

[a] Major isomer. [b] In [$^2H_6$]acetone δ from $(CD_3)_2CO$ at 30.3 p.p.m. [c] In [$^2H_4$]methanol, δ from CD_3OD at 49.0 p.p.m. [d] Tertiary carbon adjacent to aromatic rings is C-1.

The first and second steps are slow, while the final ketonization is fast; this stabilizes the final product and forces the previous equilibria to form more intermediates. An analogous tautomeric rearrangement of a quinone methide from loss of the 4-hydroxy group from flavan-3,4-diols provides an explanation for the biogenesis of 2,3-*cis*-procyanidins from 2*R*,3*R*-dihydroflavonols.[20]



Scheme 3. Rearrangement of 1-(2,4,6-trihydroxyphenyl)-3-(3,4-dihydroxyphenyl)propanone to an indan derivative

The indan derivative **(6)** it is believed is formed from **(5)** by rearrangement and dehydration, as outlined in Scheme 3. A carbanion formed from loss of a proton from C-1 attacks the carbonyl carbon of a non-aromatic tautomer of the phloroglucinol ring **(20)** to form a tertiary alcohol intermediate **(21)** which dehydrates to form the final product.

Experimental

^1H N.m.r. spectra were recorded at 80 MHz and ^{13}C n.m.r. at 20 MHz with a Varian[*] FT-80A spectrometer. Assignments of ^{13}C n.m.r. resonances were based on data provided in

---

[*] Mention of trade names does not constitute endorsement by the USDA-Forest Service.

Porter *et al.*,[12] the chemical shifts of methylene carbons of variously substituted bis-hydroxyphenylmethanes, comparisons among the chemical shifts found for the products, and, in certain instances, on results obtained from proton coupled spectra. [$^2H_6$]Acetone was used as the solvent, unless otherwise specified. F.t.–i.r. spectra were provided by Dr. T. P. Schultz, Mississippi State University, Mississippi. Mass spectral determinations were performed by the Midwest Center for Mass Spectrometry, a National Science Foundation Regional Instrumentation Facility (Grant No. CHE 8211164). Elemental analyses were performed by Galbraith laboratories.

Separations by column chromatography were done with Sephadex LH-20 packing material using 95% ethanol as the eluting solvent, unless indicated otherwise. Cellulose t.l.c. analyses were performed on Schleicher and Schull F1440 sheets in the following solvent systems; A, t-butyl alcohol–acetic acid–water (3:1:1, v/v); B, 6% acetic acid in water (v/v). Deoxygenated water was prepared by freezing distilled water (300 ml), placing the resulting ice under vacuum for 5 min, flushing with nitrogen, and then allowing the ice to melt. The alternating freezing and thawing were repeated twice. The resulting degassed water was stored under a nitrogen atmosphere. Evaporations were done using a rotary evaporator with a water-bath set at 32 °C. Acetylations were done with acetic anhydride–pyridine (1:1) at room temperature overnight.

Extraction of Loblolly Pine Phloem.—Bark collected from a loblolly pine tree [*Pinus taeda*, 10 in DBH (Diameter at Breast Height)] was steeped in acetone–water (7:3, v/v) for 72 h. The extract was then concentrated and freeze-dried to give a red-brown solid. A portion of this crude extract (50 g) was dissolved in methanol–water (1:1, v/v; *ca.* 100 ml) and applied to a Sephadex LH-20 column (2.5 × 70 cm) which was eluated with the same solvent for 16 h. The column was then eluted with acetone–water (1:1), v/v) until the eluant was no longer coloured. Evaporation and freeze-drying of the acetone–water solution gave a light brown solid. ^{13}C N.m.r. analysis of this material showed it to be relatively pure, higher-molecular weight procyanidins with little or no carbohydrate content.

Alkaline Reaction of Procyanidins with Toluene-α-thiol at 23 °C *for* 18 h.—Purified loblolly pine tannin (5.0 g) was combined with toluene-α-thiol (10 g) and deoxygenated water (75 ml). The pH was then adjusted to 12.0 by adding solid sodium hydroxide with constant magnetic stirring. During the sodium hydroxide addition, the surface of the solution was continually flushed with N_2. The resulting dark red solution was sealed in a reaction vial (100 ml) under an N_2 atmosphere and kept at 23 °C in a thermostatically controlled water-bath for 18 h.

After neutralization with dilute HCl, again under an N_2 blanket, the solution was evaporated to give a viscous, red-purple material and a colourless liquid. The unchanged toluene-α-thiol was removed by stirring the mixture with hexane (100 ml) for 10 min and then removing the hexane layer. This trituration was repeated twice further and the hexane layers discarded. The resulting product was dissolved in water along with a minimum of ethanol and then freeze-dried. The crude product was applied to a Sephadex LH-20 column (2.5 × 75 cm), packed and eluted with 95% ethanol. Tubes 40—75 were combined and evaporated to give a waxy, amorphous solid (5.14 g). This material was re-applied to a column (2.5 × 75 cm), packed and eluted with chloroform–ethanol (4:1, v/v). Fractions 77—95 were combined and evaporated to give a solid (1.8 g) which was applied to a smaller Sephadex LH-20 column (1.5 × 80 cm) eluted with chloroform–ethanol (1:1, v/v).

1,3-*Bisbenzylthio*-1-(3,4-*dihydroxyphenyl*)-3-(2,4,6-*trihydroxyphenyl*)*propan*-2-*ol* (**10**) (1.23 g) was obtained from fractions 29—36, having R_F 0.48 (streaks) and 0.72 in solvents B and A, giving a red colour with vanillin–HCl [Found: *m/z* (f.a.b.—m.s.) *M* + 1, 537.1393. $C_{29}H_{28}O_6S_2$ requires *M* + 1, 537.1406]; δ 36.4 and 37.3 (CH_2S), 48.6 (propyl C-3), 55.0 (propyl C-1), 79.2 (propyl C-2), 96.7 (C-3 + C-5, phloroglucinol), 116.1, 116.9, and 121.4 (C-2, C-5, and C-6, pyrocatechol), 107.0 and 134.5 (C-1, phloroglucinol and pyrocatechol) 127.5, 129.1, 129.9, 130.1 (tertiary phenyl), 140 (quaternary phenyl), 145—147 (C-3 + C-4, pyrocatechol), and 157—159 (C-2, C-4, and C-6, phloroglucinol); δ[$(CD_3)_2CO$] 3.38 (1 H, d, *J* 11.5 Hz, CH_2S), 3.52 (2 H, s, benzyl CH_2S), 3.6 (1 H, d, *J* 9 Hz, 3-H), 3.65 (1 H, d, *J* 11.5 Hz, benzyl CH_2S), 4.4 (1 H, dd, *J* 4, 9 Hz, 2-H), 4.65 (1 H, d, *J* 4 Hz, 1-H), 5.9 (2 H, s, phloroglucinol), 6.5 (3 H, m, pyrocatechol), and 7.1 (10 H, m, phenyl). Reaction of (**10**) with Raney Ni gave 1-(3,4-dihydroxyphenyl)-3-(2,4,6-trihydroxyphenyl)propan-2-ol.

Alkaline Reaction of Procyanidin with Toluene-α-thiol at 23 °C *for* 48 h.—The same procedure described above was used, except the reaction solution was left at 23 °C for 48 h before work-up. After dissolution in a minimum of 95% ethanol, the crude product was applied to a Sephadex LH-20 column (2.5 × 75 cm), packed and eluted with the same solvent. Fractions 27—44 were combined, evaporated, and freeze-dried to give material (1.13 g) which was re-applied to a small column of LH-20 (1.5 × 80 cm) packed and eluted with ethanol–water (1:1, v/v).

1-(3,4-*Dihydroxyphenyl*)-3-(2,4,6-*trihydroxyphenyl*)*propan*-2-*one* (**5**), (34 mg) was obtained from fractions 39—43, as a light brown amorphous solid, R_F 0.53 on cellulose t.l.c. plates developed with solvent B, initially red, fading to a purple-blue colouration with vanillin–HCl (Found: C, 59.05; H, 5.3. $C_{15}H_{14}O_6 \cdot 0.8H_2O$ requires C, 59.13; H, 5.12%) [Found: m/z (f.a.b.–m.s.) *M* + 1, 291. $C_{15}H_{14}O_6$ requires *M* + 1, 291]. ^{13}C N.m.r. showed δ: 38.1 (propyl C-3), 48.7 (propyl C-1), 96.3 (C-3 + C-5, phloroglucinol), 101.9 (C-1 phloroglucinol), 116.4, 118.2, 122.5, and 127.8 (C-2, C-5, C-6, and C-1, pyrocatechol), 145.0 and 146.0 (C-3 and C-4, pyrocatechol), 158—159 (C-2, C-4, and C-6, phloroglucinol), and 212.1 (propyl C-2 carbonyl). The f.t.–i.r. spectrum showed a C=O at 1 732 cm^{-1}; δ 3.60 (2 H, s, propyl 1-H or 3-H), 3.64 (2 H, s, propyl 1-H, or 3-H), 6.0 (2 H, s, phloroglucinol ArH), and 6.6 (3 H, m, pyrocatechol ArH).

1-*Benzylthio*-1-(3,4-*dihydroxyphenyl*)-3-(2,4,6-*trihydroxyphenyl*)*propan*-2-*one* (**11**) (131 mg) was obtained from fractions 63—69 as a light brown solid having R_F 0.60 on cellulose t.l.c. plates in solvent B, giving initially a red, then purple-red colour with vanillin-HCl [Found: *m/z* (f.a.b.–m.s.) *M* + 1, 413.1056. $C_{22}H_{20}O_6S$ requires *M* + 1, 413.1059], δ_C 36.4 and 36.2 (propyl C-3 and benzyl CH_2S), 58.2 (propyl C-1), 95.0 (C-3 and C-5, phloroglucinol), 115.8, 116.6, 121.5 (C-2, C-5, and C-6, pyrocatechol), 127.4, 128.9, 129.5 (phenyl tertiary carbons), 145 (C-3 and C-4, pyrocatechol), 157—159 (C-2, C-4, and C-6, phloroglucinol), and 206 (propyl C-2); δ 3.65 (2 H, s, propyl 3-H or benzyl CH_2S), 3.55 (2 H, s, propyl 3-H or benzyl CH_2S), 4.75 (1 H, s, propyl 1-H), 5.95 (2 H, s, phloroglucinol ArH), 6.7 (3 H, m, pyrocatechol ArH), and 7.2 (5 H, m, benzyl ArH).

1-*Benzylthio*-1-(3,4-*dihydroxyphenyl*)-3-(2,4,6-*trihydroxyphenyl*)*propan*-2-*ol* (**4**) (293 mg) was obtained from fractions 70—94 as a tan-coloured, amorphous solid with R_F 0.52 on cellulose t.l.c. plates in solvent B, giving a red colour with vanillin–HCl (Found: C, 61.25; H, 5.9; S, 7.5. $C_{22}H_{22}O_6S \cdot H_2O$ requires C, 61.11; H, 5.55; S, 7.41%) [Found: *m/z* (f.a.b.–m.s.) *M* + 1, 415. *M* + 1 requires 415]; δ_C (major isomer) 30.4 (propyl C-3), 36.8 (benzyl CH_2S), 56.9 (propyl C-1), 76.9 (propyl C-2), 96.8 (C-3 + C-5, phloroglucinol), 116.1, 117.4, and 122.7 (C-2, C-5, and C-6, pyrocatechol), 132.3 (C-1, pyrocatechol), 128.1, 129.6, and 130.4 (C-2 + C-6; C-3 + C-5; and C-4, phenyl), 145—147 (C-3 + C-4, pyrocatechol), and 156—157 (C-

2, C-4, and C-6, phloroglucinol); δ 2.56 (1 H, dd, *J* 6.5, 15.0 Hz, propyl 3-H), 2.92 (1 H, dd, *J* 2.5, 15.0 Hz, propyl 3-H), 3.53 (2 H, dd, *J* 13.5 Hz, benzyl CH_2S), 3.69 (1 H, d, *J* 8 Hz, propyl 1-H), and 4.0 (1 H, m, propyl 2-H), in addition to expected resonances for phloroglucinol, pyrocatechol, and phenyl ArH protons at 5.95 (2 H, s), 6.7 (3 H, m), and 7.2 (5 H, m). The minor isomer had carbon signals at: δ 30.0 (propyl C-3), 36.8 (benzyl CH_2S), 57.8 (propyl C-1), 77.9 (propyl C-2), and 96.9 (C-3 + C-5, phloroglucinol) with multiplicity in the lower field carbons. The ^1H n.m.r. spectrum of the minor isomer showed a similar set of signals: δ 2.46 (1 H, dd, *J* 7.5, 15.0 Hz), 3.14 (1 H, dd, *J* 2.0, 15.0 Hz), 3.53 (2 H, dd, *J* 13.5 Hz), 3.65 (1 H, d, *J* 7 Hz), 4.0 (1 H, m), and 6.0 (2 H, s). The other aromatic ring signals of the isomers could not be separated. Reaction of (4) with Raney Ni gave 1-(3,4-dihydroxyphenyl)-3-(2,4,6-trihydroxyphenyl)propan-2-ol.

Alkaline Reaction of Procyanidins with Toluene-α-thiol at 100 °C *for* 12 h.—The procedure described above was used, except for the reaction conditions of 12 h in an oven set at 100 °C. The crude product was applied to a Sephadex LH-20 column (2.5 × 75 cm), eluted with 95% ethanol. Tubes 135—145 were combined, evaporated, and re-applied to a second column (2.5 × 75 cm), again eluted with the same solvent. Fractions 21—23 gave the propan-2-one (5), physically and spectroscopically identical with that from an earlier preparation. Fractions 103—129 from the first column were also applied to a 2.5 × 75 cm Sephadex LH-20 column, packed and eluted with 95% ethanol.

1-(3,4-*Dihydroxyphenyl*)-4,6-*dihydroxyindan*-2-*one* (6) was obtained from fractions 21—35 (357 mg) of the last column above after passing through yet a further LH-20 column of this size to give finally 65 mg of product (fractions 36—40); R_F 0.71 and 0.73 on cellulose t.l.c. plates in solvents A and B; [Found: *m/z* (f.a.b.–m.s.) positive ion, $M + 1$, 273; negative ion, $M - 1$, 271; high-resolution positive ion, $M + 1$, 273.0765. $C_{15}H_{12}O_5$ requires, 273, 271, and 273.0763 respectively]; $\delta_C[(CD_3)_2SO]$: 40.6 (C-1), 58.8 (C-3), 101.6 (C-6), 103.1 (C-4), 115.5, 115.7, 119.4 (C-2, C-5, and C-6, pyrocatechol), 129.8 (C-1, pyrocatechol), 144.2, 145.1 (C-3 and C-4, catechol), and 154.2 and 157.8 (C-4 and C-6); δ 3.38 (2 H, s, 3-H), 4.37 (1 H, s, 1-H), 6.1 (1 H, d, *J* 2 Hz, 5-H), 6.35 (1 H, d, *J* 2 Hz, 7-H), and 6.5 (3 H, m, pyrocatechol ArH).

Catechin with Toluene-α-thiol under Basic Conditions.—Toluene-α-thiol (5.0 ml) was combined with 50 ml of water and the pH adjusted to 12 with solid NaOH. Catechin (2.5 g) was then added to the solution which was subsequently sealed in a reaction vial under an N_2 atmosphere and left at room temperature for 3 days. The solution was then neutralized with HCl and extracted with ethyl acetate (4 × 50 ml). The organic layers were combined, dried ($MgSO_4$), evaporated and the residue applied to a Sephadex LH-20 column (1.5 × 80 cm), packed and eluted with chloroform–ethanol (1:1, v/v). Fractions 38—66 were combined, evaporated, and freeze-dried to give a light-brown amorphous solid (1.733 g) having the same t.l.c. and spectral properties as (4) prepared from tannin. The two isomers observed previously were obtained in the same ratios as well.

1-(3,4-*Dihydroxyphenyl*)-3-(2,4,6-*trihydroxyphenyl*)*propan*-2-*ol* (18) was prepared by reductions of (4) or (10) with Raney nickel. The compound to be reduced (1g) was combined with Raney nickel (1g) in dry ethanol (5 ml) and the resulting suspension was stirred magnetically for 15 min. It was then filtered and evaporated and the product purified on a Sephadex LH-20 column (1.5 × 80 cm) using ethanol–water (3:1, v/v) as a solvent. Evaporation of fractions 30—50 gave an off-white amorphous solid (*ca.* 250 mg), R_F 0.79 and 0.61 on cellulose t.l.c. plates developed with solvents B and A, red coloration with vanillin–HCl (Found: C, 59.2; H, 5.9. $C_{15}H_{16}O_6 \cdot 0.6H_2O$ requires C, 59.4; H, 5.7%); δ_C 31.6 (C-3 propyl), 44.2 (C-1 propyl), 75.8 (C-2, propyl), 96.9 and 106.0 (C-3 and C-5, and C-1 phloroglucinol), 116.5, 118.0, 122.3, and 132.4 (C-2, C-5, C-6, and C-1, pyrocatechol), quaternaries at 144.6 and 146.1 (C-3 and C-4, pyrocatechol), and 158.2 and 158.7 p.p.m. (C-2, C-4, and C-6 phloroglucinol); δ 2.75 (4 H, m, *J* 5.0, 8.0, 9.0, 14.0 Hz, propyl 1-H and 3-H), 4.05 (1 H, m, *J* 2.5, 4.5, 5.0, 9.0 Hz, propyl 2-H), 5.95 (2 H, s, phloroglucinol ArH), and 6.7 (3 H, m, pyrocatechol ArH) [Found (for peracetate): C, 59.5; H, 4.95. $C_{27}H_{28}O_{12}$ requires C, 59.56; H, 5.15%].

References

1 P. Kiatgrajai, J. D. Wellons, L. Gollub, and J. D. White, *J. Org. Chem.*, 1982, **47**, 2910.

2 J. A. Kennedy, M. H. G. Munro, H. K. L. Powell, and L. Y. Foo, *Aust. J. Chem.*, 1984, **37**, 885.

3 L. Y. Foo and L. J. Porter, *J. Chem. Soc., Perkin Trans. 1*, 1983, 1535.

4 K. D. Sears, R. L. Casebier, H. L. Hergert, G. H. Stout, and L. E. McCandlish, *J. Org. Chem.*, 1975, **39**, 3244.

5 R. W. Hemingway and L. Y. Foo, *J. Chem. Soc., Chem. Commun.*, 1983, 1035.

6 L. Y. Foo and R. W. Hemingway, *J. Chem. Soc., Chem. Commun.*, 1984, 85.

7 F. W. Herrick, *J. Agric. Food Chem.*, 1980, **28**, 228.

8 J. J. Karchesy and R. W. Hemingway, *J. Agric. Food Chem.*, 1980, **28**, 222.

9 R. W. Hemingway, J. J. Karchesy, G. W. McGraw, and R. A. Wielesek, *Phytochemistry*, 1983, **22**, 275.

10 R. W. Hemingway, L. Y. Foo, and L. J. Porter, *J. Chem. Soc., Perkin Trans. 1*, 1982, 1209.

11 Z. Czochanska, L. Y. Foo, R. H. Newman, and L. J. Porter, *J. Chem. Soc., Perkin Trans 1*, 1980, 2278.

12 L. J. Porter, R. H. Newman, L. Y. Foo, H. Wong, and R. W. Hemingway, *J. Chem. Soc., Perkin Trans. 1*, 1982, 1217.

13 V. M. Williams, L. J. Porter, and R. W. Hemingway, *Phytochemistry*, 1983, **22**, 569.

14 M. R. Attwood, B. R. Brown, S. G. Lisseter, C. L. Torrero, and P. M. Weaver, *J. Chem. Soc., Chem. Commun.*, 1984, 177.

15 D. Jacques and E. E. Haslam, *J. Chem. Soc., Perkin Trans. 1*, 1974, 2663.

16 P. E. Laks and R. W. Hemingway, *J. Chem. Soc., Perkin Trans. 1*, in the press.

17 D. G. Roux, D. Ferreira, H. K. L. Hundt, and E. Malan, *J. Applied Polym. Sci., Polym. Symp.*, No. **28**, 1975, 335.

18 G. W. McGraw, P. E. Laks, and R. W. Hemingway, *J. Wood Chem. and Techn.*

19 R. W. Hemingway and G. W. McGraw, *J. Wood Chem. and Techn.*, 1982, **3**, 421.

20 R. W. Hemingway and P. E. Laks, *J. Chem. Soc., Chem. Commun.*, 1985, 746.

Received 4th November 1985; *Paper* 5/1928