Synthesis of high molecular mass condensed tannin by cationic polymerization of flavan 3,4-carbonate

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A new synthetic method for the preparation of high molecular mass (the highest $\overline{Mn}$† 10 200) condensed tannin has been developed. Polymerization of 3′,4′,5,7-tetrabenzyloxyflavan 3,4-carbonate **2** and subsequent debenzylation gives a condensed tannin having high molecular mass. Molecular mass of the synthetic tannin increases up to a degree of polymerization ($\overline{DPn}$) of ~35 with an increase in the reaction time. This high molecular mass condensed tannin, synthesized for the first time, is useful as a model compound for natural condensed tannins with high molecular mass, such as that from Japanese persimmon (*Diospyros kaki* L.) fruit.

Introduction

Tannins are amorphous, rarely crystalline substances which are widely distributed in the plant kingdom. They are remarkable for their astringent taste. They also have the ability to complex and to form precipitates with macromolecules such as proteins and polysaccharides, with alkaloids, and with heavy metals.[1]

Natural condensed tannin, that is, polymeric proanthocyanidin, comprising flavan-3-ol repeating units, is polydisperse with degrees of polymerization of 2–50,[2] and exists as a mixture consisting of several flavan-3-ols with different hydroxylation patterns on the A- and B-ring. Furthermore, several stereoisomers originate in the three asymmetric carbon atoms (C-2, C-3, C-4) in flavan-3-ol repeating units. Thus, the structures of natural condensed tannins are extremely complicated.[3] Such complexity has prevented the investigation of typical tannin properties, such as the interaction of condensed tannins with proteins and metal ions. Therefore, the synthetic condensed tannins with a definite structure are useful as tannin model compounds for elucidating the functions of the natural tannins.

Swain has reported that 2,3-*trans*-3,4-*cis*-flavan-3,4-diol readily polymerizes in the presence of hydrochloric acid to yield a tetramer or pentamer.[4] Fletcher *et al.* have synthesized the procyanidin dimer from 4-benzylthioflavan-3-ols prepared by thiolysis of natural procyanidin.[5] Moreover, dimer[6] or procyanidin derivatives[7] have been synthesized mainly by the condensation of flavan-3,4-diols having high reactivity for polymerization. All these starting monomers were obtained from natural products,[8] by reduction of taxifolin or by oxidation of flav-3-ene.[9] It is impossible to obtain flavan-3,4-diols with all possible hydroxylation patterns of the A- and B-ring, from natural products, for the preparation of condensed tannins.

We have established the general synthetic route for condensed tannins with all expected hydroxylation patterns in the B-ring starting from phloroacetophenone and benzaldehyde derivatives,[10] although the $\overline{DPn}$ did not exceed 3.7, and discussed the relationship between the hydroxylation pattern of the B-ring and the protein-precipitating capacity.[11]

On the other hand, in the tissues of some plants, such as ferns and the persimmon (*Diospyros kaki* L.) fruit, there are condensed tannins with expressly high molecular masses.[12] In particular, tannins of persimmon fruit (kaki tannins) have remarkable astringency and strong protein-binding capacity, but thus

far the details of their chemical structure and properties have not been clarified. This is because they are easily changed into insoluble forms, or probably transmuted during attempted purification, although there is no clear explanations for these phenomena. It has been thought that these characteristics of kaki tannins are partly attributable to the high molecularity (~ 1.38×10^4 daltons on average).[13]

Therefore, it was necessary to obtain a model condensed tannin with high molecular mass in order to elucidate the relationship between the structure and the function of natural condensed tannins such as kaki tannins. $\overline{DPn}$ of the synthetic condensed tannin, as described above, was (maximum) 3.7. Consequently, it is very important to establish the preferred synthetic method for condensed tannins with higher $\overline{DPn}$ values.

In the present paper, polymerization of flavan 3,4-carbonate yielding high molecular mass ($\overline{Mn} > 10\,000$) condensed tannins is described.

Results and discussion

Selection and preparation of flavan 3,4-carbonate 2 as a starting monomer

We have reported the general synthetic method for condensed tannins by the polymerization of benzylated flavan-3,4-diol derivatives.[10] This method is useful for the preparation of condensed tannins having the A- and B-ring with the desired hydroxylation patterns. However, it was impossible to obtain high molecular mass polymers over $\overline{DPn} = 3.7$, because the Lewis acid catalyst used is deactivated by the water released during the dehydrative polymerization of the starting flavan-3,4-diol derivatives. It is preferable to design other starting materials for the polymerization, where use would not lead to any production of molecules such as water responsible for the deactivation of the Lewis acid.

There are several coupling reactions of cyclic carbonates,[14] with the release of CO_2 which does not contribute to the drop in catalyst activity. By use of a monomer with such a cyclic carbonate structure, a condensed tannin with high molecular mass can be expected to be synthesized. Thus, we selected, 3′,4′,5,7-tetrakisbenzyloxyflavan 3,4-carbonate **2** as a new starting material, whose polymerization produces CO_2 without any inactivation effect on the Lewis acid catalyst during the polymerization.

Compound **2** was easily prepared from 3′,4′,5,7-tetrakisbenzyloxyflavan-3,4-diol **1** with *N,N′*-carbonyldiimidazole in

† $\overline{Mn}$; number-average molecular mass.
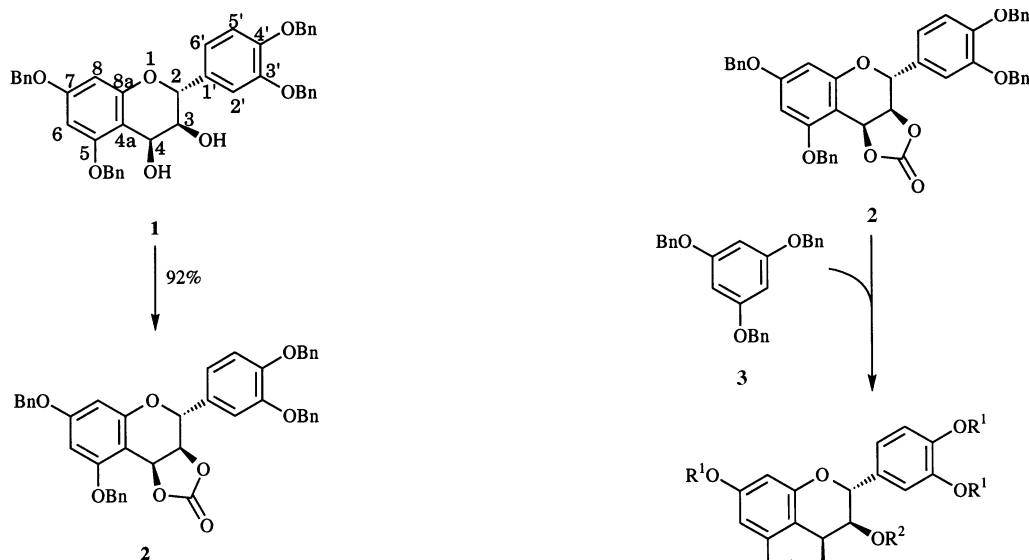
Scheme 1 *Reagent and conditions: N,N′*-carbonyldiimidazole (2 mol equiv.), benzene, reflux, 4.5 h

92% yield (Scheme 1). The structure of compound **2** was determined by an analysis of ^{1}H NMR and IR spectra. In the ^{1}H NMR spectrum, the signals for 3-OH or 4-OH of starting compound **1** disappeared. Both the signals for 3-H (δ 4.76) and 4-H (δ 5.80) appeared at lower magnetic field than those, δ 3.93 and 5.08, respectively, of compound **1**. The characteristic carbonate carbonyl absorption appearing at 1818 cm^{-1} in the IR spectrum also confirms the structure of compound **2**.
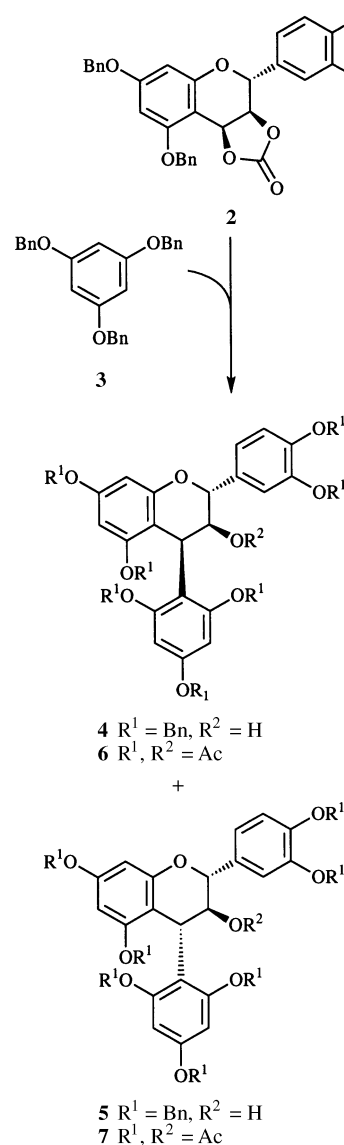
Condensation reaction of flavan 3,4-carbonate 2 with phloroglucinol tribenzyl ether 3

Prior to the condensation of compound **2** itself, we carried out a model condensation reaction of compound **2** with phloroglucinol tribenzyl ether **3** to confirm the reactivity of the cyclic carbonate function in compound **2** and to judge the relative configuration between the C-3 and C-4 positions in the condensed products.

A condensation reaction was first conducted in anhydrous CH$_2$Cl$_2$ at 0 °C in the presence of BF$_3$·Et$_2$O (0.2 mol equiv.). The reaction was found to proceed as expected and gave the desired compounds **4** (3,4-*cis* isomer) and **5** (3,4-*trans* isomer) (Scheme 2) in quantitative yield. The structures of compound **4** and **5** were identified *via* the per-acetates of 4-arylflavan-3-ols, compounds **6** and **7**, prepared by debenzylation and subsequent acetylation of compound **4** and **5**, respectively.

We then carried out the condensations under several reaction conditions using various kinds of Lewis acid (BF$_3$·Et$_2$O, TiCl$_4$, SnCl$_4$, SbCl$_5$ and Ph$_3$C$^+$ BF$_4^-$) at room temperature to −25 °C. Triphenylcarbenium tetrafluoroborate in these Lewis acids has been generally used for ring-opening polymerization in sugar chemistry. Recently, by its use, we have succeeded in the first chemical synthesis of cellulose by cationic ring opening polymerization of an orthoester.[15] The ratios of the condensation *cis*-isomer **4** and *trans*-isomer **5** were determined by the signal areas of the C-4 protons in the ^{1}H NMR spectrum: signals of C-4 protons for compounds **6** and **7** appeared at δ 4.64 and 4.59, respectively.[16]

The results are summarized in Table 1. The yield of *trans*-isomer **5** varies both with the sort of Lewis acid used and with the reaction temperature: in particular, lowering the temperature gave, on the whole, higher yields of *trans*-isomer **5**, except for the reaction using SbCl$_5$. Natural condensed tannins generally have been reported to have a *trans* C-3/C-4 configuration.[1] Highly stereoselective synthesis is important for the preparation of structurally defined condensed tannin, because the stereochemistry, especially at the C-4 position, determines the three-dimensional structure of the condensed tannin molecule.

4 R^1 = Bn, R^2 = H
6 R^1, R^2 = Ac
+
5 R^1 = Bn, R^2 = H
7 R^1, R^2 = Ac

Scheme 2 *Reagent and conditions:* phloroglucinol tribenzyl ether **3** (5 mol equiv.), Lewis acids (0.2 mol equiv.), anhydrous CH$_2$Cl$_2$, −25 °C to room temp.

Table 1 Condensation reactions of flavan 3,4-carbonate **2** with phloroglucinol tribenzyl ether **3**

Entry	Catalyst	Temp/°C	Time/h	Yield (%)	Compound 5 (%)
1	BF$_3$·Et$_2$O	RT	0.5	62^a	72
2	BF$_3$·Et$_2$O	0	1.5	94	82
3	BF$_3$·Et$_2$O	−25	24	100	94
4	TiCl$_4$	RT	1	62^a	76
5	TiCl$_4$	0	2.5	94	72
6	TiCl$_4$	−25	18	100	91
7	SnCl$_4$	RT	1	92	52
8	SnCl$_4$	0	2.5	100	38
9	SnCl$_4$	−25	20	100	60
10	SbCl$_5$	0	2.5	100	71
11	SbCl$_5$	−25	20	100	54
12	Ph$_3$C·BF$_4$	0	2.5	100	83
13	Ph$_3$C·BF$_4$	−25	20	100	93

^{a} Dimeric fraction was observed.

The favourable proportion of compound **5** attained, *i.e.*, 94 and 93%, was achieved with the reaction using boron trifluoride–diethyl ether or triphenylcarbenium tetrafluoroborate at −25 °C, respectively. In both cases, these yields are higher than that obtained in the condensation of compound **1**,

i.e., 70%.[16] Thus, the condensation reaction of compound **2** is expected to proceed more stereoselectively than that of compound **1**, although the reaction may take longer.

Polymerization of flavan 3,4-carbonate 2

Higher stereoselectivity in the condensation of compound **2** with phloroglucinol tribenzyl ether **3** at −25 °C took a longer time as described in the previous section. It is predicted that polymerization of compound **2** would take longer at this temperature than at 0 °C (for obvious reasons).

Compound **2** was polymerized in the presence of $BF_3 \cdot Et_2O$ catalyst to give a condensed product (polymer **8**) quantitively (Scheme 3). The ^{13}C NMR spectrum of polymer **8** is in good
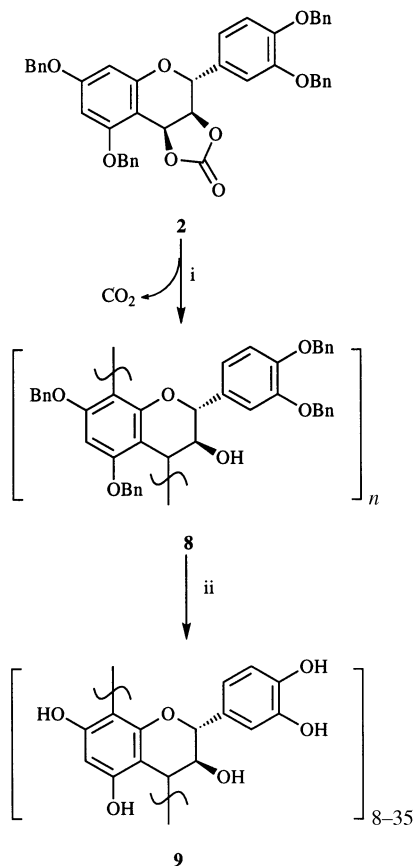
Scheme 3 *Reagent and conditions:* i, $BF_3 \cdot Et_2O$ (0.2 mol equiv.), anhydrous CH_2Cl_2, 0 °C; ii, 10% Pd–C, THF, EtOH (4 : 1), H_2, room temp., 38 h

agreement with that of the condensed tannin derivative prepared from flavan-3,4-diol **1**.[10] The IR spectrum of polymer **8** [Fig. 1(b)] was compared with that of compound **2** [Fig. 1(a)]. In the spectrum of polymer **8**, the carbonate carbonyl absorption was scarcely visible at 1818 cm^{-1}. This indicates that the polymerization of compound **2** was accompanied by elimination of CO_2.

The condensation reaction was monitored by gel permeation chromatography (GPC) (Fig. 2). The GPC patterns indicate that an increasing reaction time tends to decrease the component with the low molecule mass to give a higher molecular mass product with small polydispersity ($\overline{Mw}/\overline{Mn} = 1.49$‡) after 264 h. The polymerization proceeds during a much longer period, to reach a maximum $\overline{DPn}$ of 49 after 264 h in the present study. Consequently, it was confirmed that the Lewis acid was not deactivated in the polymerization of the cyclic carbonate **2**, a different situation from that of reaction of diol **1**, as expected. The present polymerization is useful from the point of view that the polymers with various molecular masses
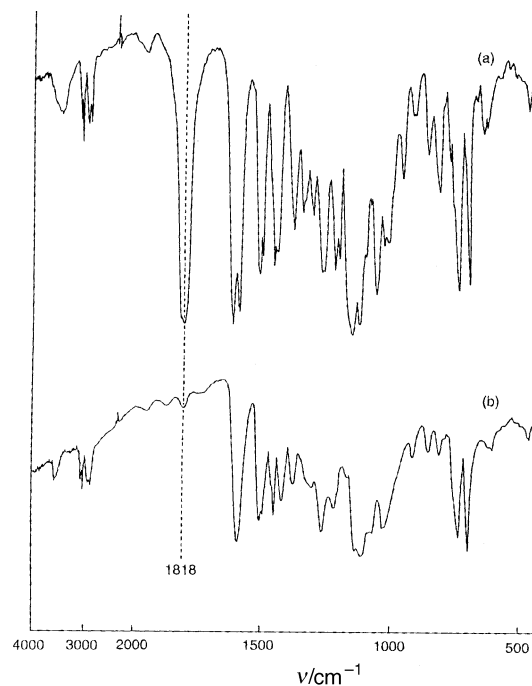
‡ $\overline{Mw}$; weight-average molecular mass.

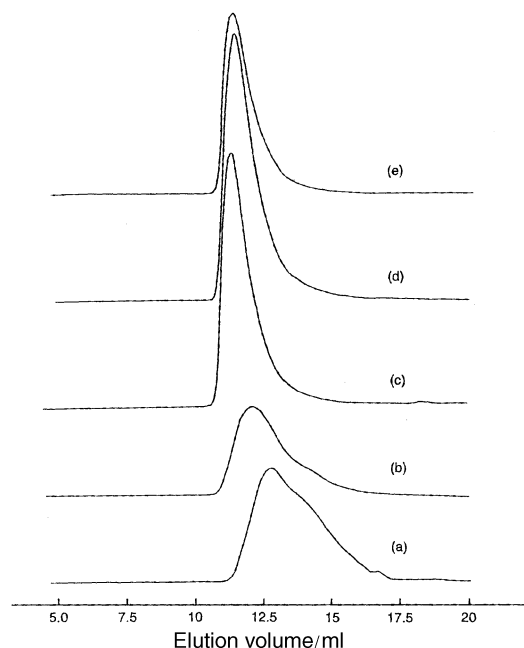**Fig. 1** IR spectra of (a) flavan 3, 4-carbonate **2** and (b) polymer **8**

Fig. 2 GPC analysis of the polymerization products **8** of flavan 3,4-carbonate **2**; (a) 24 h, $\overline{DPn} = 10$, $\overline{Mw}/\overline{Mn} = 2.01$; (b) 72 h, $\overline{DPn} = 17$, $\overline{Mw}/\overline{Mn} = 2.11$; (c) 120 h, $\overline{DPn} = 37$, $\overline{Mw}/\overline{Mn} = 1.87$; (d) 168 h, $\overline{DPn} = 40$, $\overline{Mw}/\overline{Mn} = 1.65$; (e) 264 h, $\overline{DPn} = 49$, $\overline{Mw}/\overline{Mn} = 1.49$

can be obtained by changing the reaction time. These experimental results may help initiate a study of the relationship between the functions of condensed tannin and their molecular masses.

Debenzylation was accomplished using 10% Pd–C (8 g g^{-1} of polymer **8**) in 20% ethanol–tetrahydrofuran (THF) at room temperature for 38 h. After removal of the 10% Pd–C, the solution was diluted with 1,4-dioxane, followed by freeze-drying to yield polymer **9** as a powder, which was soluble in methanol or dimethyl sulfoxide (DMSO). When the reaction mixture was worked up in a simple manner as noted in a previous report,[10] *i.e.*, filtration and evaporation, the products became insoluble in any solvent.

Complete debenzylation was confirmed by inspection of the ^{1}H NMR spectrum of the hydrogenolysis products measured in

[²H₆]DMSO; the signals derived from benzyl aromatic protons, which appear at δ ~7.3, had completely disappeared.

Under the debenzylation conditions described above, there is little possibility of the cleavage of the interflavanoid linkage or ring-opening of the C-ring by the hydrogenolysis at C-4 or C-2 in the polymer **9**; it is confirmed that debenzylation of compound **5** and elaboration gave compound **7** in quantitative yield under the same conditions as those of the synthesis of the condensed tannin **9**.

The ¹³C NMR spectrum of the acetylated synthetic condensed tannin [Fig. 3(c)] is in good agreement with that of the natural condensed tannin extracted from *Cryptomeria japonica* bark [Fig. 3(a)] and with that of the artificial condensed tannin prepared from flavan-3,4-diol **1** [Fig. 3(b)].

The stereochemistry of the synthetic condensed tannin was evaluated from its ¹³C NMR spectrum. Fig. 4 shows a part of the ¹³C NMR spectrum of the acetylated synthetic condensed tannin [Fig. 4(d)] together with three other spectra for comparison; those of two dimeric flavan-3-ols [Fig. 4(a), (b)] with 2,3-*trans*-3,4-*trans* and 2,3-*trans*-3,4-*cis* configurations, respectively, and of the acetate [Fig. 4(c)] of the condensed tannin prepared from compound **1**. According to our previous paper,[17] the signal at δ_C ~76 is characteristic for the repeating unit with 2,3-*trans*-3,4-*cis* configuration, and the signal at δ_C ~37 is for the 3,4-*trans* isomer. In spectrum [Fig. 4(d)], the signal at δ_C ~76 is small compared with that in spectrum [Fig. 4(c)]. The *cis*/*trans* ratio of the polymer **9** was calculated to be ~1:5 from the peak area and the integration values between δ_C 75–85 and δ_C ~37. The proportion of 3,4-*trans* configurational isomer of polymer **9** was higher than that of the condensed tannin prepared from compound **1** (*cis*:*trans* = 2:3). This indicates that the condensation reaction of flavan 3,4-carbonate **2** proceeded with higher stereoselectivity than did that of flavan-

3,4-diol **1**, as expected from the model condensation reactions of compound **2** with phloroglucinol tribenzyl ether **3**. Because the C-ring's stereochemistry in the natural condensed tannin has been reported to be almost completely of 3,4-*trans* configuration,[1] it is thought that the structure of the condensed tannins prepared from compound **2** are more close to that of natural tannins.

The number-average molecular mass ($\overline{Mn}$) of the acetylated synthetic condensed tannin was determined by GPC, using
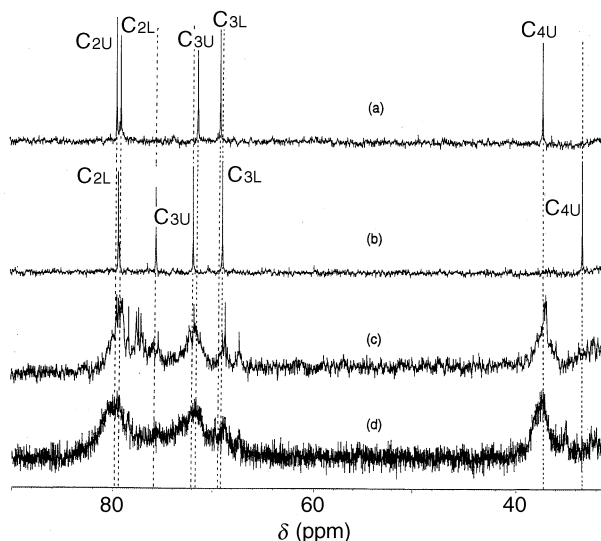

Fig. 4 ¹³C NMR spectra of procyanidine acetates; (a) 2,3-*trans*-3,4-*trans*-dimer, (b) 2,3-*trans*-3,4-*cis* dimer, (c) synthetic tannin from **1**, (d) synthetic tannin from **2**, U: Upper unit, L: Lower unit
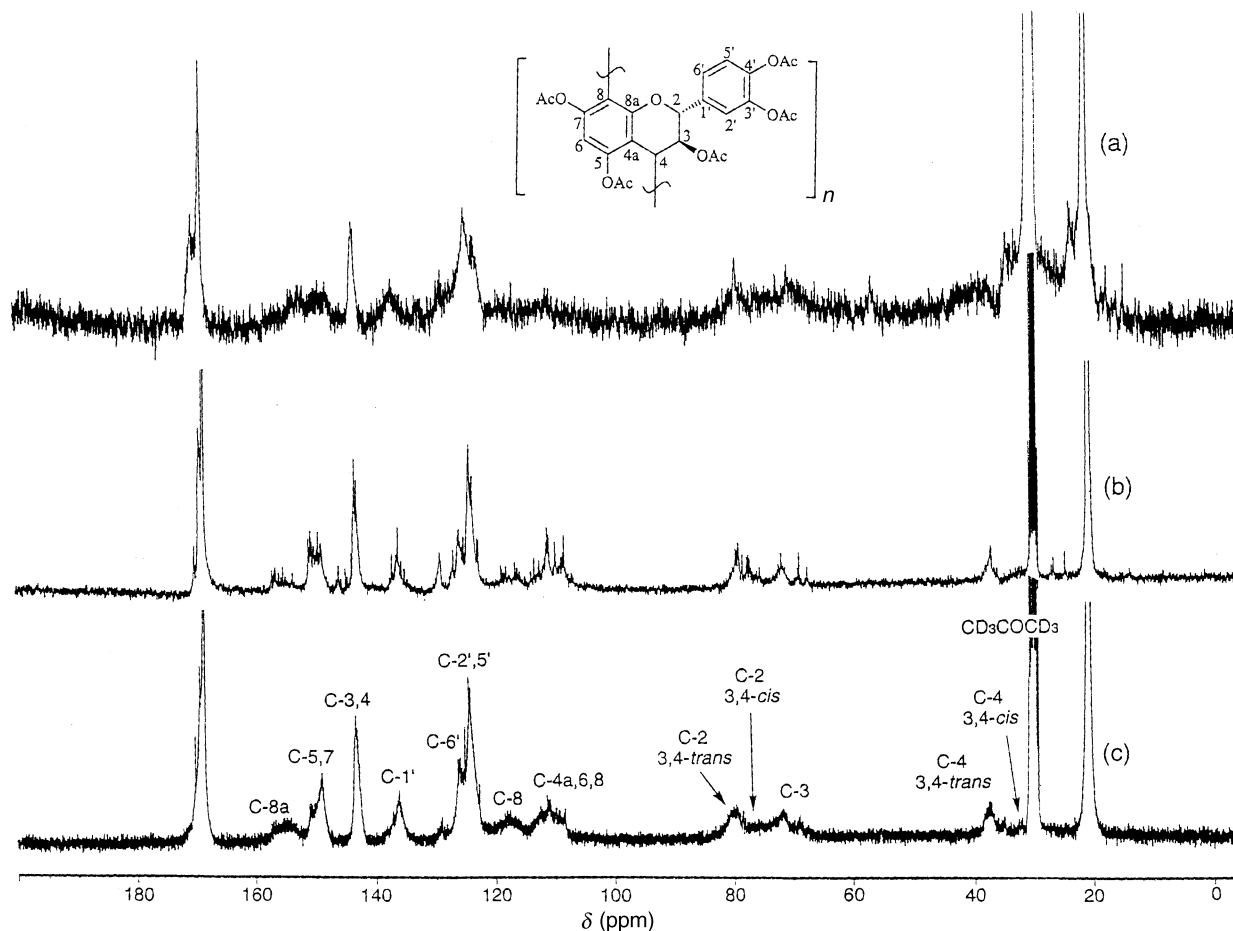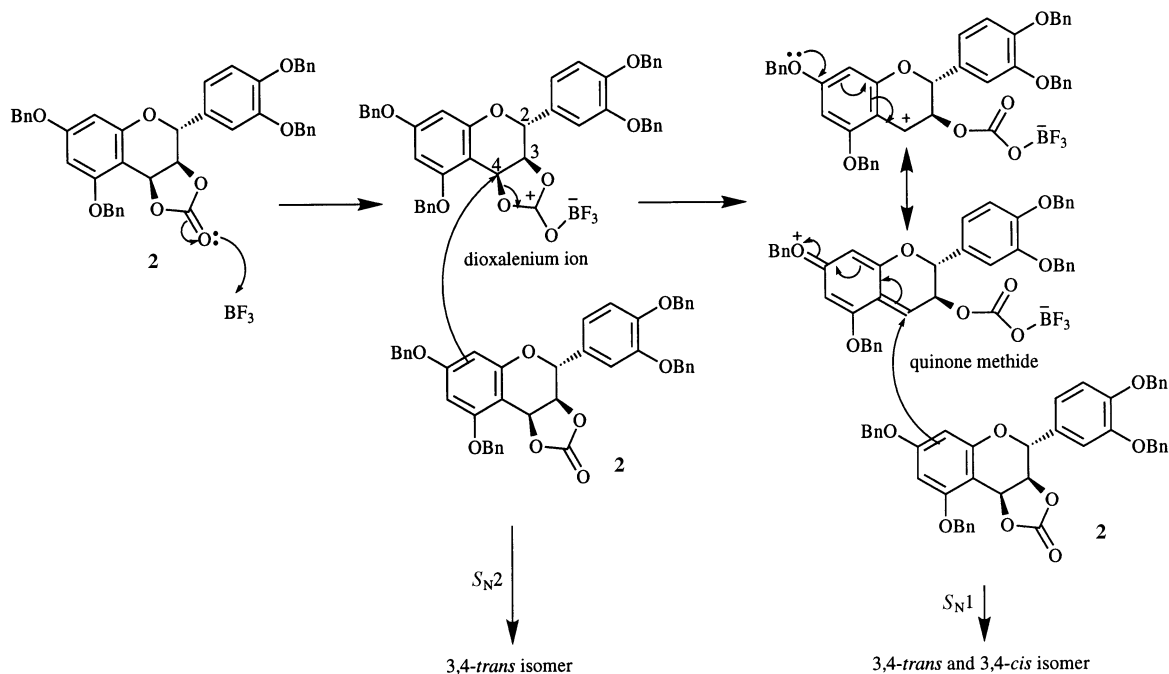

Fig. 3 ¹³C NMR spectra (75 MHz) of condensed tannin acetates; (a) *Cryptomeria japonica* bark tannin, (b) synthetic tannin from flavan-3,4-diol **1**, (c) synthetic tannin from flavan 3,4-carbonate **2**

Scheme 4

polystyrene standard, to be 3794–17 637. Thus, the molecular mass of synthetic condensed tannins were estimated to be 2209–10 200 in $\overline{Mn}$, which was calculated by subtracting the value of the acetyl groups in the acetylated preparations, corresponding to $\overline{DPn}$ of 8–35.

Thus, this synthetic method was found to be useful for the synthesis of condensed tannin derivatives with several kinds of substituent with higher molecular weights and higher stereoselectivity than those of the previous synthetic method.[10] These synthetic tannins are expected to serve the elucidation of properties of condensed tannins as the model compounds with high molecular mass, such as tannins of persimmon (*Diospyros kaki* L.) fruit.

Reaction mechanism of polymerization of flavan 3,4-carbonate 2

Polymerization of compound **2** is thought to proceed *via* the reaction mechanism shown in Scheme 4. In the initiation step of this mechanism, a dioxalenium ion intermediate is formed by the complexaion of BF_3 with the oxygen of the cyclic carbonate group. Then, an interflavan bond is formed by S_N1 or S_N2 type reaction. In cases of S_N2 reaction, the 3,4-*trans* isomer is produced by attack of the A-ring of the next monomer with Walden inversion at the C-4 position of the dioxalenium ion intermediate accompanied by the scission of C-4–O. On the other hand, both 3,4-*trans* and 3,4-*cis* isomers may be produced *via* the attack of the next monomer to the planar quinone methide intermediate.[18]

In the polymerization of compound **2**, an S_N2-type reaction is presumed to proceed judging from the product-ratio of the 3,4-*trans* and 3,4-*cis* isomers which is affected by the reaction temperature conducted. However, it is also conceivable that the 3,4-*trans* isomer may be preferentially formed in the case of the S_N1 mechanism because of the steric hindrance of the C-3 substituent group in the quinone methide intermediate.

Experimental

Mps are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were taken with a BRUKER AC300 FT-NMR (300 MHz) spectrometer with tetramethylsilane (TMS) as an internal standard in CDCl$_3$, [^{2}H$_6$]acetone- or [^{2}H$_6$]DMSO. Chemical shifts are given in δ-values (ppm and Hz, respectively). *J*-Values are given in Hz. Ultraviolet spectra were recorded with a Shimadzu

UV-365 spectrophotometer. IR spectra were recorded with a Shimadzu FT IR-4000 spectrophotometer. Anhydrous dichloromethane was distilled from P_2O_5. Molecular mass distributions of the substituted polymers were analysed by GPC in THF. A Waters universal liquid chromatograph injector (Model U6K), a Waters solvent delivery system (Model 6000A), a Waters refractive index detector (Series R-400), a Waters absorbance detector (Model 440), and Shodex columns (KF802 and KF803) were used.

Synthesis of compound 2

Compound **1** (100 mg, 0.15 mmol)[10] and *N,N′*-carbonyldiimidazole (48.7 mg, 0.30 mmol) was suspended in benzene (50 ml), and were dissolved by heating. The solution was refluxed for 4.5 h. The reaction mixture was diluted with ethyl acetate, washed with brine, dried over Na$_2$SO$_4$, and concentrated *in vacuo*. The product was purified on a silica gel column with CH$_2$Cl$_2$–*n*-hexane (2:1, v/v) to give compound **2** as crystals (95.7 mg, 92.1%), mp 162–164 °C (Found: C, 75.33; H, 5.17. C$_{44}$H$_{36}$O$_8$·0.5H$_2$O requires C, 75.30; H, 5.31%); λ_{max}(CHCl$_3$)/nm 281 (ε/dm^3 mol^{-1} cm^{-1} 7600); ν_{max}/cm^{-1} 1818 (C=O); δ_H(300 MHz; CDCl$_3$; Me$_4$Si) 4.76 (2 H, m, 2- and 3-H), 5.00–5.18 (8 H, m, PhCH_2), 5.80 (1 H, m, 4-H), 6.22 and 6.31 [2 H, 2 d, $J_{6,8}$ 2.2, Ph (A-ring)], 6.96 and 7.03 [3 H, 2 s, Ph (B-ring)], 7.25–7.46 (20 H, m, Ph); δ_C(75 MHz; CDCl$_3$) 70.17, 70.24, 70.37, 71.17, 71.48, 75.40 and 75.81 (C-2, -3, -4 and -CH$_2$Ph), 94.93, 95.14 and 98.90 (C-4a, -6 and -8), 113.97, 114.80 and 129.66 (C-2′, -5′ and -6′), 149.12, 149.78, 154.25, 157.09, 159.71 and 162.18 (C-3′, -4′, -5, -7, -8a and C=O).

Condensation reaction of compound 2 with phloroglucinol tribenzyl ether 3 and the product identification

Compound **2** (30 mg, 0.043 mmol) and phloroglucinol tribenzyl ether **3** (85.8 mg, 0.217 mmol) were dissolved in anhydrous CH$_2$Cl$_2$ (1.5 ml). BF$_3$·Et$_2$O (1.1 µl, 0.0087 mmol) was added at 0 °C. After being stirred for 1 h at that temperature, the resulting yellow-orange solution was diluted with ethyl acetate, and was washed successively with water, saturated aq. NaHCO$_3$ and brine. The organic layer was dried over Na$_2$SO$_4$ and the solvent was evaporated off *in vacuo* to yield products as a yellow oil. The resulting yellow oil was purified by TLC (CHCl$_3$) to give a mixture of compounds **4** and **5** as a light yellow oil (42.3 mg, 93.5%).

To a stirred solution of the mixture of compounds **4** and **5** (42.3 mg) in 4.3 ml of 1,4-dioxane was added 10% Pd–C (42.3 mg) and the suspension was stirred under hydrogen at 90 °C for 3 h. The reaction mixture was filtered and evaporated *in vacuo*. The resulting light yellow oil was dissolved in acetic anhydride (2 ml)–pyridine (2 ml) for acetylation. After being stirred overnight at room temperature, the reaction mixture was concentrated *in vacuo* to yield a mixture of acetylated compounds **6** and **7** (30.4 mg, ~100% yield), which were used for their structural identifications by NMR analysis.

Compound **6**: δ_H(300 MHz; CDCl$_3$; Me$_4$Si) 1.80, 1.84, 1.88 and 2.16 (12 H, 4 s, COMe), 2.27 (9 H, s, COMe), 2.28 (6 H, s, COMe), 4.64 (1 H, m, 4-H), 5.36 (2 H, m, 2- and 3-H), 6.59 and 6.70 [2 H, 2 d, $J_{6,8}$ 2.3, Ph (A-ring)], 6.90 and 6.92 [2 H, 2 d, $J_{3'',5''}$ 2.4, Ph (D-ring)], 7.19 (1 H, d, $J_{2',6'}$ 2.0, 2'-H), 7.20 (1 H, d, $J_{5',6'}$ 8.5, 5'-H) and 7.30 (1 H, dd, $J_{2',6'}$ 2.0, $J_{5',6'}$ 8.5, 6'-H); δ_C(75 MHz; CDCl$_3$) 20.34, 20.57, 20.62, 20.98 and 21.06 (COCH$_3$), 31.38 (C-4), 70.84 (C-3), 75.24 (C-2), 107.57 and 108.98 (C-6 and -8), 111.57 (C-1''), 113.47 and 114.85 (C-3'' and -5''), 118.86 (C-4a), 122.43 and 123.63 (C-2' and -5'), 124.65 (C-6'), 135.96 (C-1'), 142.25 and 141.98 (C-3' and -4'), 149.32, 149.57, 149.69, 150.02 and 150.23 (C-5, -7, -2'', -4'' and -6''), 154.34 (C-8a), 167.68, 167.95, 168.10, 168.14, 168.42, 168.78 and 170.14 (COCH$_3$).

Compound **7**: δ_H(300 MHz; CDCl$_3$; Me$_4$Si) 1.65, 1.94, 1.97, 2.23, 2.25, 2.28, 2.285 and 2.35 (24 H, 8 s, COMe), 4.59 (1 H, d, $J_{3,4}$ 9.4, 4-H), 4.90 (1 H, $J_{2,3}$ 9.9, 2-H), 5.68 (1 H, t, $J_{2,3}$ $_{3,4}$ 9.7, 3-H), 6.50 and 6.68 [2 H, 2 d, $J_{6,8}$ 2.3, Ph (A-ring)], 6.91 and 6.93 [2 H, 2 d, $J_{3'',5''}$ 2.3, Ph (D-ring)], 7.22 (1 H, d, $J_{5',6'}$ 8.4, 5'-H), 7.25 (1 H, d, $J_{2',5'}$ 1.9, 2'-H), 7.36 (1 H, dd, $J_{2',5'}$ 1.9, $J_{5',6'}$ 8.4, 6'-H); δ_C(75 MHz: CDCl$_3$) 20.25, 20.56, 20.60, 20.83, 20.98 and 21.10 (COCH$_3$), 36.72 (C-4), 71.56 (C-3), 79.46 (C-2), 108.59 and 110.30 (C-6 and -8), 113.36, 114.70 and 114.85 (C-1'', -3'' and -5''), 121.28 (C-4a), 122.95 and 123.50 (C-2' and -5'), 125.43 (C-6'), 134.55 (C-1'), 141.83 and 142.48 (C-3' and -4'), 149.04, 149.17, 149.33 and 149.99 (C-5, -7, -2'', -4'', -6''), 155.67 (C-8a), 167.16, 167.91, 167.97, 168.12, 168.18, 168.28, 168.65 and 168.86 (COCH$_3$).

Condensations using other Lewis acids (TiCl$_4$, SnCl$_4$, SbCl$_5$, Ph$_3$C·BF$_4$) were also conducted in a similar manner to that described above.

Polymerization of compound 2

The polymerization should be conducted under completely anhydrous conditions. For this purpose, a simple vacuum system[19] was used. BF$_3$·Et$_2$O (3.6 µl, 0.029 mmol) was added to a solution of compound **2** (100 mg, 0.145 mmol) in anhydrous CH$_2$Cl$_2$ (750 µl) at 0 °C. After being stirred for the prescribed time (24–264 h), the resulting purple red solid was dissolved in CHCl$_3$. The solution was diluted with ethyl acetate and washed successively with water, saturated aq. NaHCO$_3$ and brine. The organic layer was dried over Na$_2$SO$_4$ and the solvent was evaporated *in vacuo* to yield condensed product **8** as a colourless solid (94.0 mg, ~100%).

Debenzylation of condensed product 8

Condensed product **8** (47.8 mg) was hydrogenated on 10% Pd–C (382.4 mg) in THF/EtOH (4:1; 5 ml) at room temp. for 38 h. Pd–C was removed from the reaction mixture by centrifugation at 3500 rpm for 10 min and twice washed with methanol (5 ml). The combined supernatant solutions were concentrated *in vacuo* at below 35 °C to about 2 ml. The solution obtained was diluted with 1,4-dioxane (20 ml) and freeze-dried for 24 h to yield condensed tannin **9** as a solid (15.8 mg, 73.8%).

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