The Metabolism of Gallic Acid and Hexahydroxydiphenic Acid in Plants. Part 3.[1] Esters of (*R*)- and (*S*)-Hexahydroxydiphenic Acid and Dehydrohexahydroxydiphenic Acid with D-Glucopyranose ($^1C_4$ and Related Conformations)

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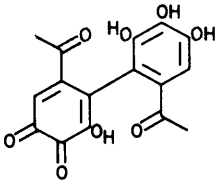
In a small group of plants a process of further metabolism of galloyl-D-glucose esters occurs in which oxidative coupling takes place between galloyl ester groups in the 1,6:2,4 or 3,6-position of D-glucopyranose in its least favoured $^1C_4$ (*C*-1) or related skew-boat conformations. This group also metabolise esters of dehydrohexahydroxydiphenic acid (1).

SURVEYS [2] of the phenolic metabolites of the leaves of higher plants show that the most commonly encountered patterns of metabolism of gallic acid are (i) the formation of simple esters with sugars, polyols, and other phenols,[3] (ii) the formation of depsides (group A),[3] and (iii) the formation of (*S*)-hexahydroxydiphenoyl esters by oxidative coupling of vicinal galloyl ester groups (4,6 and 2,3) attached to D-glucopyranose in its most stable $^4C_1$ (1-*C*) conformation [4] (group B).[1,5] According to present evidence [2,5] a rather smaller group of plants adopts a further metabolic variation in which oxidative coupling of adjacent galloyl ester groups occurs 1—3 to form both (*R*)- and (*S*)-hexahydroxydiphenoyl esters in a D-glucopyranose precursor which itself adopts the less favourable $^1C_4$ (*C*-1) or an intermediate skew-boat conformation. An additionally significant feature of this last form of metabolism is that one or more of the hexahydroxydiphenoyl ester groups, in key metabolites, may be further dehydrogenated to give derivatives of the dehydrohexahydroxydiphenoyl ester group (1). Phenolic metabolites



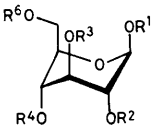
(1)

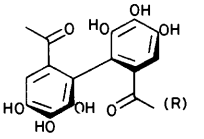
of this class (group C) have been discerned [2] in members of the plant families Cercidiphyllaceae, Ericaceae, Onagraceae, Combretaceae,[6] Nyssaceae, Aceraceae,[7] Punicaceae, Simaroubaceae, and Geraniaceae.[8]

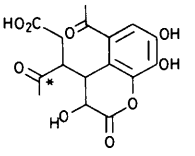
For its routine metabolic processes Nature appears to prefer the conformationally most stable sugars and amongst the D-hexoses the three most stable ones glucose, mannose, and galactose are very widely distributed. Those with higher free energies occur rarely, if ever. It is a point of some curiosity, therefore, that in this particular form of oxidative metabolism of galloyl esters of D-glucose transformations apparently occur with the galloyl-D-glucopyranose precursor in an energetically unfavourable chair ($^1C_4$; *C*-1) or related skew boat conformation. The difference in free energy between the $^1C_4$ (*C*-1) and $^4C_1$ (1-*C*) forms of D-glucopyranose is calculated [4] as +5.95 kcal mol^{-1} (24.8 kJ mol^{-1}) and this difference may in part explain why oxidative coupling of galloyl ester groups *via* the $^4C_1$ (*C*-1) form (class B) of the D-glucopyranose precursor is much more widely encountered in plants than that *via* the alternative $^1C_4$ (1-*C*) or skew-boat forms (class C). As yet [2] only one plant, *Fuchsia* sp. (Onagraceae), has been detected where both classes of metabolite coexist.

In an earlier paper [1,5] it was shown that the chirality of a hexahydroxydiphenoyl ester group attached to D-glucopyranose ($^4C_1$, 1-*C*) could be predicted assuming that it was biosynthetically derived by oxidative coupling of two vicinal galloyl ester groups. Using a similar approach it may be predicted that 3,6-coupling in a galloyl D-glucopyranose ($^1C_4$, *C*-1) will preferentially form the *R*-configuration and 1,6-coupling the corresponding *S*-configuration in the derived hexahydroxydiphenoyl ester group. This prediction is confirmed for the 3,6-coupled product by measurements [9] which show the chirality of the hexahydroxydiphenoyl ester group in corilagin (2) to be *R*. In contrast both *R* and *S* configurations appear equally accessible in 2,4-oxidative coupling. However in both instances the two aroyl rings adopt an almost orthogonal relationship which leads (*vide infra*) to facile hydrolysis.

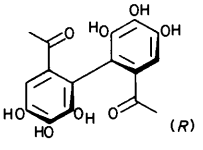
The structural analysis of this class of phenolic metabolite is based both on the ^{13}C and ^1H n.m.r. criteria established earlier for esters of hexahydroxydiphenic acid [1,5] and upon a study of D-glucopyranose derivatives in which the sugar adopts the $^1C_4$ (1-*C*) or a derived boat conformation. The crystal structures of both 1,6-anhydro-D-glucopyranose [10,11] [laevoglucosan, (11)] and its triacetate [12] have recently been reported and they show the pyranose ring to adopt a strained 1-*C* conformation in which all the substituent groups adopt a quasi-axial orientation. Acetylation of laevoglucosan 'flattens' the pyranose ring [12] such that the distance of C-3 from the mean plane defined by C-1, 2, 4, and 5 is decreased by 0.05 Å. Slight flattening of the pyranose ring in the direction of a sofa conformation is also observed in the crystal structure of 3-amino-1,6-anhydro-3-deoxy-β-D-glucopyranose (12).[13] In the ^1H n.m.r. spectrum [14,15] of (12) the same conformational features of the molecule are reflected in the low vicinal coupling constants of the hydrogens 1-H to 5-H (1—2 Hz) and

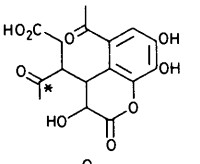


(2) R^1 = CO·C_6H_2·$(OH)_3$ − 3,4,5 ; $R^2 = R^4 = H$; R^3, R^6 =  Corilagin

(3) $R^1 = R^3 = R^6$ = CO·C_6H_2·$(OH)_3$ − 3,4,5 ; R^2, R^{4*} =  Chebulinic acid

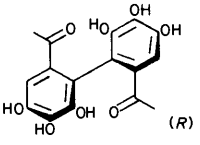
(4) R^1 = CO·C_6H_2·$(OH)_3$ − 3, 4, 5

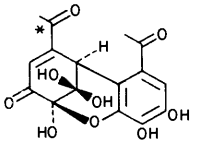
R^3, R^6 = 

R^2, R^{4*} = 

Chebulagic acid

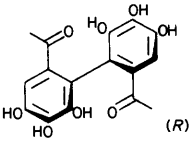
(5) R^1 = CO·C_6H_2·$(OH)_3$ − 3, 4, 5 ;

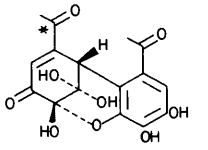
R^3, R^6 = 

R^2, R^{4*} = 

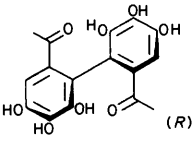
Geraniin

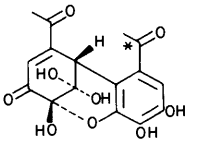
(6) R^1 = CO·C_6H_2·$(OH)_3$ − 3, 4, 5 ;

R^3, R^6 = 

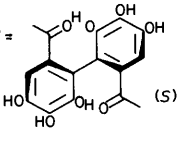
R^2, R^{4*} = 

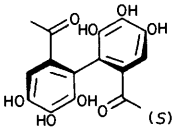
(7) R^1 = CO·C_6H_2·$(OH)_3$ − 3, 4, 5 ;

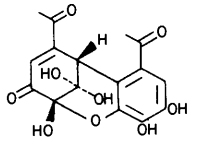
R^3, R^6 = 

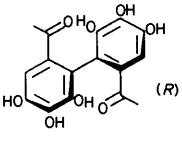
R^2, R^{4*} = 

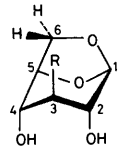
(8) $R^2 = R^3 = R^4$ = CO·C_6H_2·$(OH)_3$ − 3, 4, 5 ;

R^1, R^6 = 

(9) R^1, R^6 = 

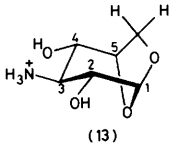
R^2, R^4 = 

(10) R = CO·C_6H_2·$(OH)_3$ − 3,4,5 ; $R^2, R^4 = R^3 R^6$ = 

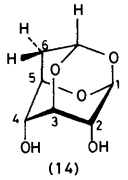


(11) R = OH

(12) R = NH_2



(13)

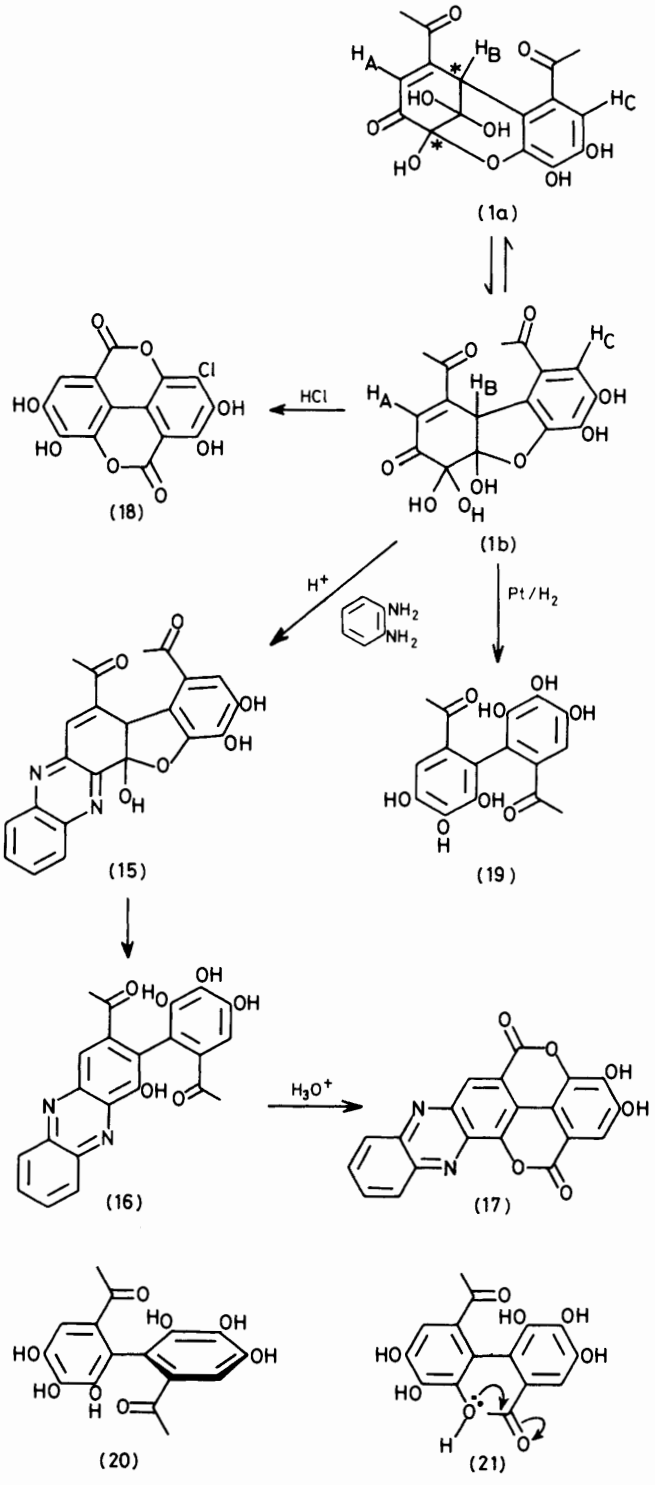


(14)

the relatively high long-range couplings ($J_{1,3}$; $J_{2,4}$; $J_{3,5}$) characteristic of the familiar planar 'W' arrangement of atoms.[16] Jochims, Taigel, and Meyer zu Reckendorf [17] used the trioxa-adamantane (14) as a model for the D-glucopyranose molecule in the $^4C_1$ (1*C*) conformation and observed vicinal and long-range coupling constants for the protons 1-H to 5-H in broad agreement with the values obtained for laevoglucosan and its derivatives [14,15] (Table 2). The divergences from the predicted values for vicinal coupling constants $J_{1,2}$, $J_{2,3}$, $J_{3,4}$, and $J_{4,5}$ for (13) based on the Karplus equation were attributed to the influence of substituents, different bond lengths in the ring, and to the effect of lone-pair electrons on the ring oxygen atoms.[16,17] This general pattern of ^{1}H coupling constants has been used as a basis for the recognition of the $^1C_4$ (1*C*) conformation in this group of phenolic metabolites. In the case of the hydrochloride of the 3-amino-derivative (13) high coupling constants (*ca.* 8.0 Hz) were found for $J_{2,3}$ and $J_{3,4}$ and correspondingly very low values (0—1.0 Hz) for $J_{1,2}$ and $J_{3,5}$ such as to suggest that this salt adopts a boat (B_{03}) conformation for the pyranose ring (13).[16] This pattern of coupling constants has similarly been used as a model to delineate boat-type conformations of the sugar ring in this class of phenolic metabolite.

Chebulinic acid (3) and chebulagic acid (4) are two well authenticated phenolic metabolites derived from the dried fruit of *Terminalia chebula* (Myrabolans, Combretaceae). Earlier ^{1}H n.m.r. analysis by Schmidt and his collaborators [18] suggested a flexible ($1B \rightleftharpoons B3$ or 1*C*) conformation for corilagin (2) and chebulinic acid (3) and a 1*C* conformation for chebulagic acid (4). These observations have been amplified and partly corroborated in this work (Table 2) using 400 MHz ^{1}H n.m.r. analysis with proton decoupling. The pattern of coupling constants observed is consistent with the adoption of a 1*C* conformation by chebulagic acid (4). But for both corilagin (2) and chebulinic acid (3) the patterns of coupling constants are best interpreted in terms of similar 1*C* conformations with possibly some flattening of the pyranose rings at C-1 and the ring oxygen (O-5) respectively.

Schmidt [19] first isolated and described the unusual dehydrohexahydroxydiphenoyl ester group (1) in two compounds brevilagin 1 and 2 from the dried fruit pods of *Caesalpinia brevifolia* (Algarobilla, Leguminosae). More recently Okuda [9,20-23] has shown the same structural entity to be present in terchebin, [20] (previously isolated by Schmidt [24] from Myrobalans), in the yellow crystalline geraniin (5), from *Geranium thunbergii* and other *Geranium* and *Euphorbia* species [21,22] and in mallotusinic acid from *Mallolotus japonicus*.[23] A distinctive characteristic of the dehydrohexahydroxydiphenoyl ester group in geraniin (5) and the brevilagins is its isomerisation in hydroxylic media. This produces in the ^{1}H and ^{13}C n.m.r. spectra a complex pattern of signals due to the various isomeric forms present in solution (Table 3). Several explanations have been favoured [21,22] since Schmidt's original observations [19,24] but most recently Okuda has analysed the ^{13}C n.m.r. data in terms of the proposition that in the molecule of geraniin in solution the dehydrohexahydroxydiphenoyl ester group exists predominantly as an equilibrium mixture of the two hydrated cyclic hemi-acetal forms (1a) and (1b). Both Schmidt [19,24] and Okuda [21] characterised the dehydrohexahydroxydiphenoyl ester group by its hydrolysis with



concentrated hydrochloric acid to give chlorellagic acid (18) and by its condensation with *o*-phenylenediamine to give sequentially the phenazines (15) (Okuda's latest formulation) and (16). Hydrolysis of the latter in boiling water gives the phenazine bis-lactone (17) and, in the case of geraniin, the residual phenolic fragment of corilagin (2). This evidence along with the spectroscopic data leads to the overall formulation of geraniin in the crystal form as (5). The orientation of the positions of esterification of (1a) to the D-glucopyranose ring was based on the reaction of the phenazine derivative (15) with moist diazomethane which cleaves the ester linkage at C-2 specifically.[21]

In this work geraniin was obtained from the leaves of

TABLE 1

D-Glucopyranose ($^1C_4$) and related boat conformations, ^{1}H (D-glucose): chemical shifts (δ, $SiMe_4$)

Compound *	1-H	2-H	3-H	4-H	5-H	6-H	6-H	Solvent
1,6-Anhydro-D-glucose (11)	5.36	3.43	3.59	3.59	4.55	4.00	3.65	D_2O [14]
	5.44	3.51	3.66	3.66	4.61	4.07	3.74	D_2O
	5.19	3.22	3.44	3.35	4.38	3.98	3.54	$(CD_3)_2SO$ [15]
	5.90	4.12	4.47	4.08	4.86	4.39	3.81	C_5D_5N
β-1-*O*-Galloyl-3,6-(*R*)-hexahydroxydiphenoyl-D-glucose (corilagin) (2)	6.21	3.95	4.62	4.20	4.20	4.20	4.20	$(CD_3)_2SO$ [18]
Corilagin undeca-acetate	6.32	5.22	4.90	5.44	4.57	4.84	4.40	$CDCl_3$
Chebulinic acid (3)	6.56	5.52	6.37	5.00	4.76	4.91	4.78	$(CD_3)_2CO$
	6.68	5.58	6.55	5.13	←4.60→		4.27	$(CD_3)_2CO$–C_5D_5N
	6.30	5.27	6.10	5.01	←4.4—4.9→			$(CD_3)_2SO$ [18]
Chebulagic acid (4)	6.52	5.52	5.96	5.23	4.82	4.78	4.43	$(CD_3)_2CO$
	6.29	5.32	5.63	4.98	← 4.70 →			$(CD_3)_2SO$ [18]
β-1,6-(*S*)-Hexahydroxydiphenoyl-2,3,4-tri-*O*-galloyl-D-glucose (8)	6.12	5.79	5.52	5.20	4.58	4.85	4.43	$(CD_3)_2CO$
β-1,6-(*S*)-Hexahydroxydiphenoyl-2,3,4-tri-*O*-galloyl-D-glucose (8) pentadeca-acetate	6.21	5.42	5.84	5.06	4.65	4.80	4.50	$CDCl_3$
β-1-*O*-Galloyl-2,4:3,6-bis-(*R*)-hexahydroxydiphenoyl-D-glucose (10)	6.17	5.57	5.21	5.45	4.80	4.72	3.99	$(CD_3)_2CO$
β-1-*O*-Galloyl-2,4:3,6-bis-(*R*)-hexahydroxydiphenoyl-D-glucose (10) pentadeca-acetate	6.07	5.70	5.23	5.58	4.78	5.00	4.05	$CDCl_3$
β-1-*O*-Galloyl-3,6-(*R*)-Hexahydroxy-2,4-dehydrohexahydroxydiphenyl-D-glucose	6.55	5.40—5.60	4.67—5.00	5.40—5.60	4.28	4.67–5.00	5.40—5.60	$(CD_3)_2CO$ [21]
(Geraniin) (5) (a)	6.59	5.58	5.51	5.55	4.82	4.96	4.35	$(CD_3)_2CO$
(Geraniin) (5) (b)	6.58	5.59	5.50	5.43	4.80	4.79	4.45	$(CD_3)_2CO$
(a)	6.55	5.55	5.35	5.48	4.80	4.80	—	$(CD_3)_2CO$–10% D_2O
(b)	6.50	5.48	5.35	5.52	—	—	—	$(CD_3)_2CO$–10% D_2O
(a)	6.57	5.59	5.50	5.54	◄4.75——4.95►		4.35	$(CD_3)_2CO$–10% CF_3CH_2OH
(b)	6.58	5.60	5.40	5.60	—	—	—	$(CD_3)_2CO$–10% CF_3CH_2OH
Geraniin-phenazine (16)	6.14	5.63	5.48	5.48	4.99	4.72	4.03	$(CD_3)_2CO$ [21]
	6.18	5.69	5.55	5.45	5.02	4.80	4.06	$(CD_3)_2CO$
Granatin B (a)	6.58	5.21	5.51	5.94	4.85	5.28	4.26	$(CD_3)_2CO$
(isomeric with geraniin) (b)	6.57	5.12	5.60	6.23	4.85	5.30	4.22	
(6) or (7)								
Granatin B-phenazine (16)	6.50	5.08	5.43	5.59	4.82	4.75	4.31	$(CD_3)_2CO$
β-1,6-(*S*)-Hexahydroxydiphenoyl-2,4-dehydrohexahydroxydiphenoyl-D-glucose,* (9)	6.08	5.0—5.20	4.60	5.0—5.20	4.10	4.50	4.60	$(CD_3)_2CO$
β-1,6-(*S*)-Hexahydroxydiphenoyl-2,4-dehydrohexahydroxydiphenoyl-D-glucose,* (9) phenazine (15)	5.90	5.01	4.60	4.91	—	—	—	$(CD_3)_2SO$
β-1,6-(*S*)-Hexahydroxydiphenoyl-2,4-dehydrohexahydroxydiphenoyl-D-glucose,* (9) phenazine (16)	5.88	5.00	4.69	5.00	—	—	—	$(CD_3)_2SO$, 7 days
β-1,6-(*S*)-Hexahydroxydiphenoyl-2,4-dehydrohexahydroxydiphenoyl-D-glucose,* (9) phenazine (15)	6.60	5.59	5.20	5.46	4.45	5.90	4.91	C_5D_5N
β-1,6-(*S*)-Hexahydroxydiphenoyl-2,4-dehydrohexahydroxydiphenoyl-D-glucose,* (9) phenazine (16)	6.52	5.54	5.01	5.01	4.35	6.09	5.01	C_5D_5N, 24 h

* Dehydrohexahydroxy-diphenoyl group—equilibrated species.

(a) and (b) Refer to the two hemiacetal forms of the dehydrohexahydroxydiphenoyl ester group (1a) and (1b).

various *Geranium* sp.[2], *Acer* sp.,[2,7] *Fuchsia* sp.,[2] and *Cercidiphyllum japonicum*[2] and it has been identified in other plant species.[2] Okuda favoured the 1*B* conformation for the D-glucopyranose ring of geraniin[22] but the more detailed high-resolution ^{1}H n.m.r. experiments reported here (Tables 1 and 2) show that the was derived from its smooth catalytic reduction to the 2,4:3,6-bis-(*R*)-hexahydroxydiphenoyl-D-glucose derivative (10) and its slow hydrolysis (water, 90 °C $t_{\frac{1}{2}}$ *ca.* 24 h) to corilagin (2) and 3,6-(*R*)-hexahydroxydiphenoyl-D-glucose. The reduction product (10) adopts a skew-boat conformation, analogous to that of the phenazine deriv-

TABLE 2

D-Glucopyranose ($^1C_4$) and related boat conformations ^{1}H (D-glucose): coupling constants (Hz)

Compound	1,2	2,3	3,4	4,5	5,6		6,6	1,3	2,4	3,5	1,4	Solvent
1,6-Anhydro-D-glucose (11)	1.7	~2.0	—	2.2	1.0	5.8	7.5	1.3	1.3	—	—	D_2O [14]
	1.8	2.5	—	1.3	1.2	5.7	7.6	1.3	1.3	—		D_2O
	1.2	2.6	2.4	2.3	1.1	5.9	7.1	1.4	1.1	1.2	—	$(CD_3)_2SO$ [15]
	1.2	3.2	3.2	1.4	1.2	5.8	7.2	1.2	1.2	1.4		C_5D_5N
Trioxa-adamantane (14) [17]	1.9	3.9	4.0	1.3 1.5	1.5	4.8	13.1	1.9	1.1	~0.7	1.0	
Corilagin (2)	6.8	1—2	≈2	1—2	—	—	—	—	<1	—	—	$(CD_3)_2SO$ [18]
Corilagin undeca-acetate	3.6	≈1	2.2	≈1	—	—	—	—	—	—	—	$CDCl_3$ [18]
	2.0	2.0	2.0	0.5	7.5	7.5	12.5	0.5	0.5	—	—	$CDCl_3$
Chebulinic acid (3)	≈4.3	≈1.4	≈3.0	≈1.0	—	—	—	—	≈1.0	—	—	$(CD_3)_2CO$
	2.7	1.5	3.6	0.9	—	—	—	0.9	1.0	0.9	—	$(CD_3)_2CO$
Chebulagic acid (4)	2.3	1—2	≈3.0	1—2	—	—	—	<1	—	—	<1	$(CD_3)_2SO$ [18]
	1.5	2.2	3.8	1.0	10.0	9.5	10.0	0.9	1.2	1.0	~0.4	$(CD_3)_2CO$
β-1,6-(*S*)-Hexahydroxydiphenoyl-2,3,4-tri-*O*-galloyl-D-glucose (8)	2.5	7.0	7.0	2.0	2.0	4.0	11.0	—	—	—	—	$(CD_3)_2CO$
β-1,6-(*S*)-Hexahydroxydiphenoyl-2,3,4-tri-*O*-galloyl-D-glucose (8) pentadeca-acetate	2.5	7.0	7.0	2.0	2.0	4.0	11.0	—	—	—	—	$CDCl_3$
β-1-*O*-Galloyl-2,4:3,6-bis-(*R*)-hexahydroxydiphenyl-D-glucose (10)	6.0	≈0	3.5	≈0	3.5	8.0	12.0	—	—	—	—	$(CD_3)CO$
β-1-*O*-Galloyl-2,4:3,6-bis-(*R*)-hexahydroxydiphenyl-D-glucose (10) penta-deca-acetate	6.0	≈0	3.0	≈0	4.0	8.0	12.0	—	—	—	—	$CDCl_3$
Geraniin (5), β-1-*O*-galloyl-3,6(*R*)-Hexahydroxydiphenoyl-2,4-dehydrohexahydroxydiphenoyl-D-glucose (a + b)	1.0	2.5	3.5	1.5	8.0	11.0	11.0	1.0	1.0	1.2	0.9	$(CD_3)_2CO$
Geraniin-phenazine (16)	6.0	—	—	—	4.0	9.0	12.0	—	—	—	—	$(CD_3)_2CO$ [21]
	6.0	≈0	3.5	≈0	4.0	8.0	11.0	—	—	—	—	$(CD_3)_2CO$
*Granatin B (6) or (7), (a + b) (isomeric with geraniin)	1.2	3.3	3.2	1.3	9.5	10.0	11.0	1.2	1.2	1.2	1.0	$(CD_3)_2CO$
Granatin B-phenazine (16)	1.5	2.0	2.0	0.5	6.0	7.0	11.0	—	—	—	—	$(CD_3)_2CO$

* 1,5 coupling ≈ 1.0 Hz.

(a) and (b) Refer to the two hemiacetal forms of the dehydrohexahydroxy-diphenoyl ester group (1a) and (1b).

pattern of coupling constants is similar to that for chebulagic acid (4) and hence supports the alternate suggestion of the 1*C* conformation for the D-glucopyranose ring. The observations on the isomerisation of the dehydrohexahydroxydiphenoyl ester group (1a) ⇌ (1b) are presented here in more detail. Although the rate of change in hydroxylic media is enhanced the chemical shift (Table 1) and coupling constant (Table 2) data are very similar for the two major species such as to suggest very little change in the shape of the molecule as it undergoes isomerisation. The ^{13}C n.m.r. changes are consistent with Okuda's explanation.[22] In addition the changes in the region of the spectra associated with the various C-4 atoms of the aroyl rings (δ **135—139** p.p.m.) shows that the isomerisation involves changes in the chemical environment of just one such atom—presumably C-4 of the ester (1). Further proof of the geraniin structure (5) ative of geraniin (16) (Tables 1 and 2) and is consistent with the development of the *R*-configuration in the derived 2,4-hexahydroxydiphenoyl ester group and the adoption of a conformation in which the D-glucopyranose anomeric proton lies in the shielding zone of one of the aromatic nuclei (upfield chemical shift of 1-H). It is interesting to note the facile hydrolytic cleavage ($t_{\frac{1}{2}}$ *ca.* ½ h, water, 90 °C) of the 2,4-hexahydroxydiphenoyl group from both the reduction product (10) and the phenazine derivative (16) to give corilagin (2) in practically quantitative yield. This contrasts strongly with the relative stability to hydrolysis of the 2,4-linked dehydrohexahydroxydiphenoyl ester group and of the hexahydroxydiphenoyl group when it is linked 3,6-, 2,3-, and 4,6- to D-glucopyranose. Co-occurring with geraniin (5) in all the plant sources examined is a substance isomeric with geraniin which is named isogeraniin. It

shows all the properties consistent with the presence of a dehydrohexahydroxydiphenoyl ester group (1) in the molecule (isomerisation, phenazine formation, and reduction). It is quantitatively transformed by refluxing in water (1 h) to geraniin and in deuterium oxide this occurs without incorporation of deuterium into the product. Its relationship to geraniin has not yet been clarified.

are, however, substantial differences in chemical shift (Table 1) for the D-glucopyranose protons in granatin B (6) or (7), its isomerisation product, and phenazine derivatives (16) when compared with those of geraniin (5). In addition, the pattern of coupling constants for the phenazine of granatin B (6) or (7) show that this derivative retains a conformation of the pyranose ring similar to to that of the parent compound (Table 2).

TABLE 3

^{1}H Chemical shifts and coupling constants of the dehydrohexahydroxydiphenoyl group (δ values from $SiMe_4$, J values in Hz)

Compound *		H_A	H_B	H_C	Solvent
Geraniin (5)	(a)	6.53 (s)	5.16 (s)	7.13 (s)	$(CD_3)_2CO$ [21]
	(b)	6.26 (d, J 1.5)	4.72 (d, J 1.5)		
	(a)	6.47 (s)	5.12 (s)	7.16 (s)	$(CD_3)_2CO$
	(b)	6.20 (d, J 1.3)	4.88 (d, J 1.3)	7.19 (s)	
Granatin B (6) or (7)	(a)	6.60 (s)	5.08 (s)	7.22 (s)	$(CD_3)_2CO$
	(b)	6.30 (d, J 1.3)	4.97 (d, J 1.3)	7.26 (s)	
β-1,6-(*S*)-Hexahydroxydiphenoyl-2,4-Dehydrohexahydroxydiphenoyl-D-glucose (9)	(a)	6.53 (s)	5.58 (s)	7.28 (s)	$(CD_3)_2CO$
	(b)	6.20 (d)	5.00 (d)	7.21 (s)	
Terchebin [19]	(a)	6.48 (s)	4.96 (s)	7.15 (s)	$(CD_3)_2SO$
	(b)	6.24 (d)	4.66 (d)	7.22 (s)	
Brevilagin 2 [19](a), (b)		6.5 (d ~ 1.0)	4.63 (d ~ 1.0)	6.94 (s)	$(CD_3)_2SO$

* (a) and (b) Refer to the two hemiacetal forms of the dehydrohexahydroxydiphenoyl ester group (1a) and (1b).

Very recently Okuda [22] has reported in a preliminary way the isolation of two further dehydrohexahydroxydiphenoyl ester metabolites from the fruit shell of *Punica granatum*—granatins A and B, (9) and (6) respectively. Outline evidence in favour of the structures has been presented. We have isolated 1,6-(*S*)-hexahydroxydiphenoyl-2,4-dehydrohexahydroxydiphenoyl-D-glucose (9) [the orientation of the ester group, (1), has not been determined] from the leaves of *Punica* sp. and *Davidia involucrata* (dove tree), and a yellow crystalline substance, isomeric with geraniin, and which on the basis of the evidence is identical with granatin B described by Okuda.[22] Granatin B forms a phenazine derivative (16) analogous to that formed from geraniin and on hydrolysis (water, 90 °C, 2 h) this yields the phenazine bis-lactone (17), corilagin (2), and 3,6-hexahydroxydiphenoyl-D-glucose. Hydrolysis with concentrated hydrochloric acid gives ellagic and chlorellagic acids (18). Catalytic reduction of granatin B yields a range of products amongst which is a substance (*ca.* 10%) provisionally identified as (10) on the basis of paper chromatography. The crude reduction product yields corilagin (2) upon hydrolysis. Further confirmation of the presence of the dehydrohexahydroxydiphenoyl ester group (1) is given by the ^{1}H n.m.r. data (Table 3) and ^{13}C n.m.r. which show a similar isomerisation to that displayed by geraniin. The pattern of coupling constants for the D-glucopyranose protons of granatin B (Table 2) is again consistent with a 1*C* conformation for the sugar ring similar to geraniin. There

The c.d. spectrum of both geraniin and granatin B are dominated by the c.d. chromophore of the corilagin (2) part structure.[25] However when the c.d. spectrum of corilagin is subtracted from that of geraniin and granatin B the difference spectra are mirror-image curves. This gives further support to the proposal made by Okuda,[22] on the basis of the relative mutarotations observed for geraniin and granatin B, that the dehydrohexahydroxydiphenoyl groups in these metabolites are enantiomeric at the centres marked *. The aromatisation which occurs when *O*-phenylenediamine condenses with the group (1) in both geraniin and granatin B produces changes in shape in the C-2, C-4 bridged linkage. These changes can best be interpreted if the resultant biphenyl derivative (phenazine or reduction product) is formed by a process which involves the least motion of atoms in the residue (1). Making this assumption the chirality of the hexahydroxydiphenoyl phenazine group (16) in the geraniin derivative is (*R*) and that from granatin B is (*S*). The same arguments lead to the prediction of the *R* configuration for the 2,4-hexahydroxydiphenoyl ester group in the reduction product (10) from geraniin and this proposal is supported by c.d. data.[25] The substantial upfield chemical shift (Table 1) of 1-H and 4-H in the phenazine derivatives (16) of geraniin and granatin B respectively, when compared with the parent compounds, is then readily explicable. Molecular models thus show that in the respective phenazine derivative these protons now fall in the shielding zone of one of

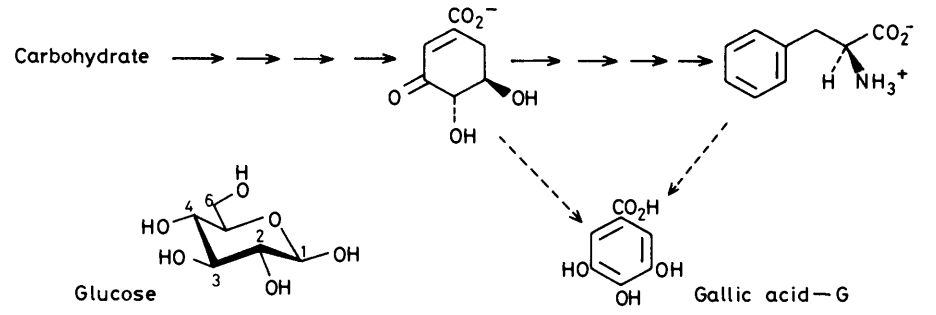
the aromatic nuclei of the newly formed biphenyl system.

The question of the orientation of the dehydrodiphenoyl ester group in granatin B on the D-glucopyranose ring has not been definitively solved. Biogenetic considerations and the analogies to both chebulinic acid (3) and chebulagic acid (4) favour a similar orientation to that proposed [22] for geraniin (5). However molecular models show that the carbonyl function of the ester groups at C-2 and C-4 are the major influence on chemical environment, and hence chemical shift, of 2-H and 4-H (Table 1). The juxtaposition of these groups with respect of 2-H and 4-H in both geraniin and granatin B is very similar and there is no indication from models why there should be such substantial differences in chemical shift for the aliphatic protons 2-H and 4-H in the two metabolites (Table 1), unless it is that the dehydrohexahydroxydiphenoyl ester is linked in the opposite orientation in granatin B, *e.g.* (7). Okuda [22] favours the formulation with the ester groups linked as in geraniin and these suggestions are based primarily on the reaction of the phenazines (16) with moist diazomethane. These reactions proceed with the hydrolysis of the ester linkage at C-2 in the geraniin derivative and at C-4 in the granatin B derivative and this evidence is, paradoxically, interpreted in terms of an identical orientation of the bridging dehydrohexahydroxydiphenoyl ester group.[22]

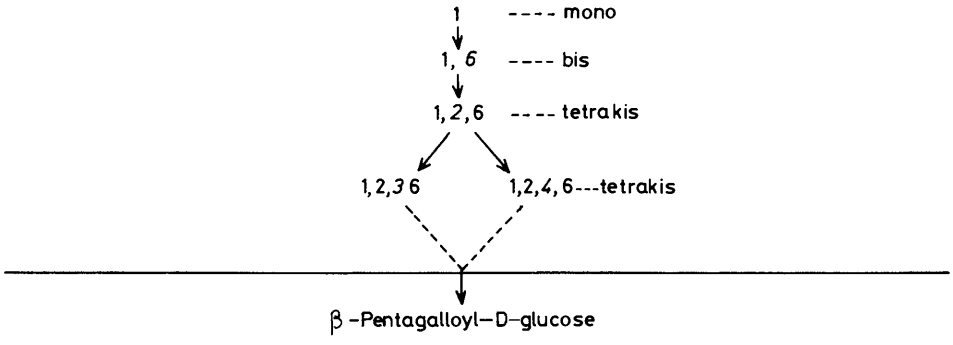
From the phenolic extract of leaves of *Davidia involucrata* (Dove tree) two compounds have been isolated in which oxidative coupling of galloyl ester groups of the presumed galloyl-D-glucose precursor occurs *via* the 1,6-positions. C.d. data [25] show that the hexahydroxydiphenoyl ester group in β-1,6-hexahydroxydiphenoyl-2,3,4-trigalloyl-D-glucose (8) has the predicted (*vide supra*) *S* configuration and ^{1}H n.m.r. measurements show that the molecule and its acetate derivative adopt a skew-boat conformation (related to B-3), Table 2. The 1,6-orientation of the hexahydroxydiphenoyl ester group was deduced on the basis of its *S*-configuration, the conformation adopted by the D-glucopyranose ring and hydrolysis experiments. In water at 90 °C the metabolite decomposes (24—48 h) to give a series of galloyl esters of D-glucose (paper chromatographic identification). No additional hexahydroxydiphenoyl esters were detected and this is consistent with a structure in which one of the points of attachment of the hexahydroxydiphenoyl ester group is at the anomeric centre C-1, since previous observations [26] show ester hydrolysis to proceed most rapidly at this point. A further metabolite which contains the dehydrohexahydroxydiphenoyl ester group (1) has been obtained from *Davidia involucrata* and *Punica granatum* and is formulated provisionally as (9)—β-1,6-(*S*)-hexahydroxydiphenoyl-2,4-dehydrohexahydroxydiphenoyl-D-glucose. C.d. measurements [25] show the hexahydroxydiphenoyl ester group to possess the *S*-configuration and the dehydrohexahydroxydiphenoyl ester group the same configuration as in granatin B. Hydrolysis of the metabolite occurred at 90 °C in water but no further hexahydroxydiphenoyl ester derivatives were detected, indicating once again the probable attachment of the hexahydroxydiphenoyl group, at one point, to the anomeric centre. Hydrolysis with concentrated hydrochloric acid gave ellagic and chlorellagic acids (18). The phenazine derivative (15) crystallised from acetonitrile solution and changed with time (the reaction was followed by ^{1}H n.m.r., Table 1) in [$^2H_5$] pyridine (24 h) or $(CD_3)_2CO$–D_2O (7 days) to the phenazine derivative (16). A distinctive feature of the ^{1}H n.m.r. spectrum of the phenazine derivative (16) in [$^2H_5$]pyridine is the chemical shift of one of the diastereotopic 6-H protons. This has been attributed to the through-space effect of the development of a partial anionic charge on the hydroxy-group at C-3. This observation then leads to the overall structural formulation (9). Reduction of (9), as with granatin B, does not lead to the formation of a single reduction product.

One of the two distinctive features of this group of phenolic metabolites is the occurrence of the 2,4-linked hexahydroxydiphenoyl ester group in its dehydro-form (1) and this particular facet appears worthy of further brief comment. Hydroxy-*o*-benzoquinones are normally reactive systems but in (1) stabilisation is achieved by intramolecular hemiacetal formation. The two aromatic nuclei of a hexahydroxydiphenoyl ester group when it bridges the 2,4-positions of D-glucopyranose are constrained to an almost orthogonal relationship (20). This conformation facilitates hydrolysis by neighbouring group participation (21) and thus $t_{\frac{1}{2}}$ (H_2O, 90 °C) for the 2,4-linked hexahydroxydiphenoyl ester group in (10) is *ca.* ½ h. Dehydrogenation of one phenolic nucleus and stabilisation by internal hemiacetal formation converts the hexahydroxydiphenoyl ester into a very stable grouping [$t_{\frac{1}{2}}$ (H_2O, 90 °C) *ca.* 24 h]. If molecules such as geraniin have pertinent biological functions or roles to play then this device may be a simple means to ensure their longer term survival in the plant tissue.

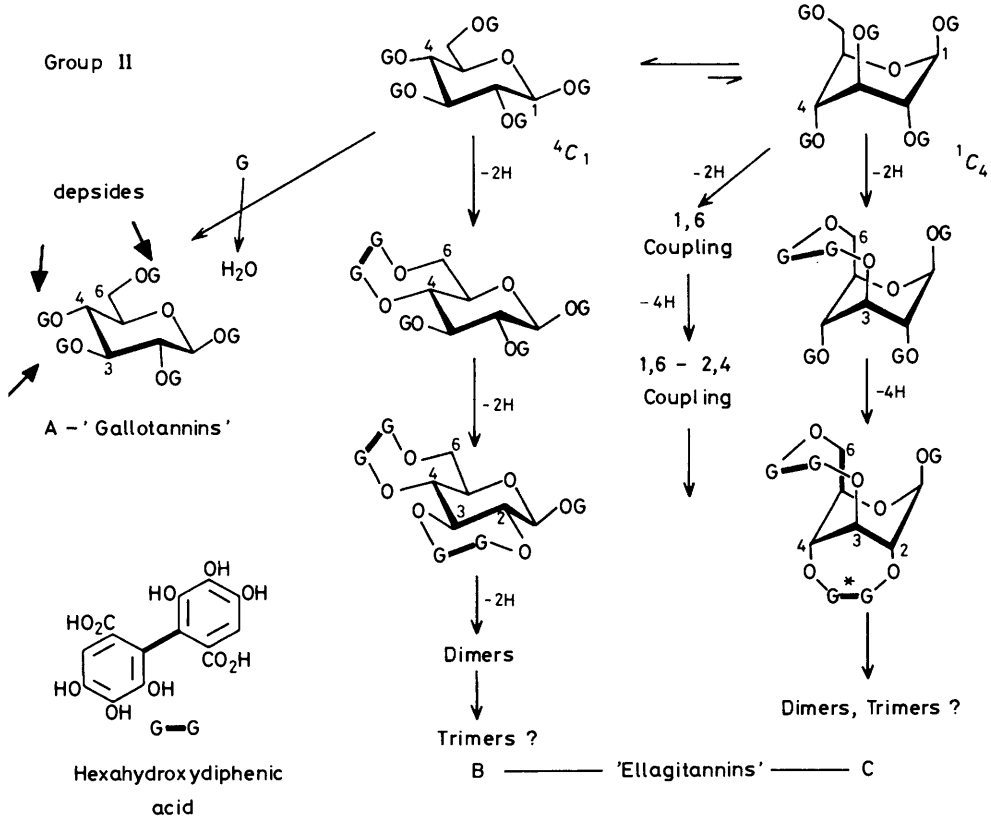
This paper and the two preceding ones summarise the principal structural patterns discerned amongst gallic acid metabolites found in the *leaves* of higher plants. These patterns represent a classic example of the biosynthetic prodigality evident in secondary metabolism. One key compound (gallic acid) is visualised as being formed (see Scheme). This then undergoes a wide range of chemical modifications leading to a plethora of secondary metabolites each one only slightly different from the next. A reasonable explanation of the phenomenon is that it results from an accumulation of intermediates in the shikimate pathway [27] of aromatic amino-acid biosynthesis at some stage during growth. Enzymes are then induced for the synthesis of a secondary product (gallic acid) from intermediates in this pathway. One class of plants (group 1, Scheme) simply converts this secondary product to esters with D-glucose (usually). Three further classes (groups 11A, 11B and 11C, Scheme) subsequently metabolise the key intermediate β-penta-*O*-galloyl-D-glucose in three separate and distinct ways—by the addition of further depsidically bound gallic acid groups (11A, Scheme, gallotannins), by oxida-



Group I



Group II



tive metabolism *via* the $^4C_1$ conformation (11B, Scheme, ellagitannins) and by oxidative metabolism *via* the $^1C_4$ conformation (11C, Scheme, ellagitannins).

EXPERIMENTAL

General Methods.—Chromatographic and isolation procedures were as previously described.[3] Hexahydroxydiphenoyl esters and their derivatives were characterised by a spray of nitrous acid.[1] Glucose was determined by a modification [26] of the method of Park and Johnson [28] after hydrolysis of the natural phenolic ester with the adaptive enzyme tannase.[26,29]

Geraniin (5).—This compound was isolated from leaves of *Geranium robertanium* (Herb Robert), *G. pratense* (Meadow Cranesbill), *G. lucidium* (Shining cranesbill), *Acer pseudoplatanus* (Sycamore), *A. monspessulanum*, *A. griseum*, *A. palmatum*, and *Cercidiphyllum japonicum* and crystallised as yellow needles from methanol–water, m.p. >300 °C (Found: C, 50.4; H, 3.5. Calc. for $C_{41}H_{26}O_{26}\cdot 2H_2O$: C, 50.7; H, 3.1%), $[\alpha]_D^{20}$ −138° (*c* 0.7 in methanol), after 4 days at 20 °C $[\alpha]_D^{20}$ −100°; R_F(A) 0.17, R_F(B) 0.21. The ^{13}C n.m.r. ([$^2H_6$]acetone $SiMe_4$) showed after dissolution (1 h) peaks at δ 191.8 (CO), 168.5, 166.2, 165.5, 165.3, and 164.9 (ester CO), 139.8, 138.9, 137.8, and 136.5 (C-4 of galloyl and hexahydroxydiphenoyl groups), 96.2 and 92.3 (2×); 90.8, 72.5, 70.0, 65.9, 63.3, and 62.9 (glucose C), and 46.1 p.p.m. After 24 h at 30 °C additional peaks were apparent at δ 194.4 (CO), 137.4 (C-4 hexahydroxydiphenoyl group), 91.8; 73.3, 70.5, 66.9, 63.7, and 62.4 (glucose C), and 52.0 p.p.m. Addition of D_2O or CF_3CH_2OH caused no change in the spectrum.

Hydrolysis of geraniin (30 h, H_2O, 90 °C) gave, after chromatography of the products in ethanol on Sephadex LH-20, corilagin (2) which gave small needles (*ca.* 10% yield) from water, m.p. 200—205 °C (decomp.) (lit.,[30] m.p. 204—205 °C) (Found: C, 49.4; H, 4.0. Calc. for $C_{27}H_{22}O_{18}\cdot H_2O$: C, 49.7; H, 3.7%), $[\alpha]_D^{20}$ −226° (*c* 0.8 in ethanol), R_F(A) 0.40, R_F(B) 0.28; ^{13}C n.m.r. ([$^2H_6$]acetone $SiMe_4$) δ 164.9 (galloyl CO), 168.5 and 167.1 (hexahydroxydiphenoyl CO), 139.1, 137.1, and 136.6 (C-4-aroyl ester), 94.1 (C-1 glucose), 75.6 (C-5), 70.4 (C-3), 68.9 (C-2), 64.8 (C-4), and 62.1 p.p.m. (C-6). The acetate of corilagin (acetic anhydride–pyridine, 24 h) crystallised from ethyl acetate–methanol as small prisms, m.p. 212—215 °C (lit.,[30] m.p. 211—212 °C), $[\alpha]_D^{20}$ −24.5° (*c* 0.5, $CHCl_3$); the nonamethyl ether (diazomethane) separated as needles from methanol, m.p. 227—229 °C (lit.,[30] m.p. 227 °C), $[\alpha]_D^{20}$ −140°. 3,6-(*R*)-Hexahydroxydiphenoyl-D-glucose, R_F(A) 0.81; R_F(B) 0.26 was obtained from the hydrolysis as a pale brown amorphous solid.

Hydrolysis of geraniin with 10M-hydrochloric acid (10 min reflux) gave, on cooling, an off-white granular precipitate which was collected and washed with water and dried at 100 °C, (0.05 mmHg) (Found: Cl, 5.2. Calc. for $C_{14}H_6O_8$ + $C_{14}H_5ClO_8$: Cl, 5.5%).

The phenazine derivative (16) of geraniin was obtained by dissolving the phenol (0.20 g) in acetonitrile (30 ml) and treating it with a solution of freshly sublimed *o*-phenylenediamine (0.03 g) in glacial acetic acid (3.0 ml). After 18 h at 20 °C the solution was reduced at 30 °C to a yellow gum which was triturated with water and the precipitate collected by filtration. The product was crystallised from methanol–chloroform to give a bright yellow powder (0.15 g), m.p. >280 °C (Found: C, 52.9; H, 3.40; N, 2.6. Calc. for $C_{47}H_{30}N_2O_{24}\cdot 3H_2O$: C, 53.2; H, 3.4; N, 2.6%), $[\alpha]_D^{20}$ −98° (*c* 0.5 in MeOH); ^{13}C n.m.r.; δ ($SiMe_4$) 164.7 (galloyl CO), 166.4, 166.1, 167.8 and 168.2 (hexahydroxydiphenoyl CO), 91.7 (glucose C-1), 76.8 (2×), 68.7, 67.7, and 65.3 p.p.m. (D-glucose-5C).

The phenazine derivative (16) (0.75 g) in methanol (5 ml) and water (75 ml) was refluxed for 2½ h. The deep-red precipitate was collected and crystallised from acetone to give small red needles of the phenazine bis-lactone (17) (0.06 g), m.p. >275 °C (Found: C, 64.2; H, 2.4; N, 7.2. Calc. for $C_{20}H_8N_2O_6$: C, 64.5; H, 2.2; N, 7.5%), ^1H n.m.r. (CF_3CO_2D) δ ($SiMe_4$) 8.02 (1 H, s), 8.20—8.82 (m, 4 H), and 9.60 (s, 1 H). Removal of the solvents from the filtrate after the separation of compound (17) gave, by chromatography on Sephadex LH-20, corilagin (0.27 g) which was identified and characterised as above.

Hydrogenation of Geraniin.—Geraniin (0.75 g) was dissolved in ethanol (25 ml) and hydrogenated at room temperature and pressure over 5% Pd–C for 24 h. The solution, after separation of the catalyst, was chromatographed on Sephadex LH-20 to give β-1-O-*galloyl*-2,4:3,6-*bis*-(R)-*hexahydroxydiphenoyl*-D-*glucose* (10) (0.54 g) as a pale brown solid after repeated evaporation from anhydrous acetone (Found: C, 51.3; H, 3.4. $C_{41}H_{28}O_{26}\cdot H_2O$ requires C, 51.6; H, 3.1%); R_F(A) 0.41; R_F(B) 0.25; ^{13}C n.m.r. δ($SiMe_4$) 168.2, 167.9, 167.2, and 166.1 (hexahydroxydiphenoyl ester CO), 164.9 (galloyl ester CO), 139.5, 139.0, 136.4, 136.2, and 136.0 (C-4 aroyl ester groups), 91.9 (glucose C-1), and 77.0, 76.1, 67.8, 67.8, and 65.3 p.p.m. (glucose 5-C). Hydrolysis (H_2O, 90 °C, ½ h) and chromatography of the products on Sephadex LH-20 gave corilagin (80%) characterised and identified as above.

The pentadeca-acetate (prepared in acetic anhydride–pyridine) crystallised from methanol as a white powder, m.p. 204—208 °C (Found: C, 54.5; H, 3.7. $C_{71}H_{62}O_{41}$ requires C, 54.4; H, 3.7%), $[\alpha]_D^{20}$ +34.5° (*c* 0.8 in Me_2CO).

Isogeraniin.—Isogeraniin was isolated, in comparable amounts to geraniin, from the phenolic extracts of leaves of *Geranium* and *Acer* sp. as a pale yellow solid (Found: C, 49.5; H, 3.6. $C_{41}H_{26}O_{26}\cdot H_2O$ requires C, 49.8; H, 3.2%), $[\alpha]_D^{20}$ −100° (*c* 0.8 in Me_2CO); R_F(A) 0.17, R_F(B) 0.24; ^1H n.m.r. ([$^2H_6$]acetone $SiMe_4$) δ 7.20 (galloyl, s, 2 H), 7.10, 7.17, and 6.68 (hexahydroxydiphenoyl 3 H), 6.56 (bs, 1 H, glucose 1-H), 5.52, 5.58, and 5.41 (bs 3 × 1 H, glucose 2-,3-,4-H, 4.75—4.90, 4.00, and 4.30—4.45 (3 H, m, glucose 5-H, 6-H_2); ^{13}C n.m.r. ([$^2H_6$]acetone $SiMe_4$) δ 194.4, 192.0, and 191.7 (CO), 168.3, 166.1, 165.5, 165.4, and 164.6 (aroyl ester CO), 139.7, 138.8, 137.8, 136.5, and 137.3 (C-4 aroyl ester), 91.7 and 90.7, 73.3 and 72.7, 70.0 and 69.9, 66.0 and 65.8, 63.8 and 63.7, and 62.4 (glucose C), 52.1, 48.5, and 46.2.

Hydrolysis (H_2O, 90 °C, 30 h) gave gallic acid, ellagic acid, 3,6-(*R*)-hexahydroxydiphenoyl-D-glucose, and corilagin which were isolated and identified as described above. Heating isogeraniin in water (90 °C, ½ h) gave geraniin (>85%) which was isolated and crystallised from methanol–water. When the reaction was conducted in deuterium oxide the geraniin which was isolated contained *no* non-exchangeable deuterium.

Treatment of isogeraniin with *o*-phenylenediamine in acetonitrile–acetic acid solution (as above for geraniin) gave a phenazine derivative (16) which separated from acetone–chloroform as a pale yellow powder, m.p. >250 °C (Found: C, 54.0; H, 3.3; N, 3.1. $C_{47}H_{30}N_2O_{24}\cdot 2H_2O$ requires C, 54.2; H, 3.3; N, 2.7%). Paper chromatography (solvent

system B[3]) showed the phenazine to consist of at least three components, the principal one of which was identical to the phenazine derivative (16) of geraniin.

Hydrolysis of isogeraniin (10M-hydrochloric acid, 10 min) gave a mixture of ellagic and chlorellagic acids (Found: Cl, 5.2. Calc. for $C_{14}H_6O_8$ + $C_{14}H_5ClO_8$: Cl, 5.5%).

Granatin B (6) *or* (7).—Granatin B was isolated from the leaves and the fruit shell of pomegranate, *Punica granatum*. The phenol crystallised from water as orange rosettes, m.p. >285° (decomp.) (Found: C, 51.9; H, 3.3. Calc. for $C_{41}H_{26}O_{26}\cdot H_2O$: C, 51.7; H, 2.9%), $[\alpha]_D^{20}$ −103° (*c* 0.7 in Me_2CO); R_F(A) 0.16, R_F(B) 0.14. ^{13}C n.m.r. ([$^2H_6$]acetone/$SiMe_4$) δ values after 1 h: 191.7 (CO), 168.8, 166.8, 165.7 (2×), 164.8 (aroyl ester CO), 139.7, 138.8, 137.9, and 136.3 (C-4 aroyl ester groups), 96.3 and 92.8 (2×); 91.0 (glucose C-1), 72.6, 69.9, 64.0 (2×), and 61.3 (5 C-glucose), and 46.4 p.p.m. After 24 h at 30 °C additional peaks were observed at δ 194.2 (CO), 137.3 (C-4 aroyl ester group), 91.3 (glucose C-1), 73.1, 70.3, 65.1, and 62.3 (5C-glucose), and 51.9 p.p.m.

Hydrolysis of granatin B (water, 90 °C, 36 h) gave, after chromatography of the products on Sephadex LH-20 in ethanol, 3,6-(*R*)-hexahydroxydiphenoyl-D-glucose and corilagin (2) (5%) which were identified by the methods described above. Treatment of granatin B with 10M-hydrochloric acid gave ellagic and chlorellagic acids (Found: Cl, 4.8. Calc. for $C_{14}H_6O_8$ + $C_{14}H_5ClO_8$: C, 5.5%).

The *phenazine* derivative (16) of granatin B was prepared in acetonitrile (*vide supra* geraniin) and separated from methanol–chloroform as a yellow powder, m.p. >270 °C (d.) (Found: C, 52.8; H, 3.7; N, 2.2. $C_{47}H_{30}N_2O_4\cdot 3H_2O$ requires C, 53.2; H, 3.4; N, 2.6%). Hydrolysis of the phenazine (16) from granatin B in methanol–water (*vide supra* geraniin) at 90 °C for 2 h gave the phenazine bislactone (17) and corilagin (2) (40%) identified and characterised as above.

β-1,6-(S)-*Hexahydroxydiphenoyl*-2,3,4-*trigalloyl*-D-*glucose*.—The *phenolic metabolite* was isolated from leaves of *Davidia involucrata* (dove tree) as a buff coloured powder after repeated evaporation from anhydrous acetone (Found: C, 52.3; H, 3.70. $C_{41}H_{30}O_{26}$ requires C, 52.5; H, 3.20%), $[\alpha]_D^{20}$ +37° (*c* 0.7, MeOH), R_F(A) 0.15, R_F(B) 0.21; ^1H n.m.r. ([$^2H_6$]acetone/$SiMe_4$) δ 7.11, 7.14, and 7.16 (3 × 2 H, s, galloyl), 6.85 and 6.87 (2 × 1 H, s, hexahydroxydiphenoyl); ^{13}C n.m.r. δ ($SiMe_4$) 168.2 and 166.2 (hexahydroxydiphenoyl ester CO), 165.6 (galloyl ester CO), 94.0, 74.8, 70.7, 70.1, 68.7, and 64.8 p.p.m. (glucose-C).

The *pentadeca-acetate* was prepared in acetic anhydride–pyridine and separated from methanol as small white prisms, m.p. softens 180—190 °C, melts 225—227 °C (decomp.) (Found: C, 53.7; H, 3.9. $C_{71}H_{60}O_{41}$ requires C, 54.3; H, 3.8%), $[\alpha]_D^{20}$ −14.2° (*c* 1.2, $CHCl_3$); ^1H n.m.r. δ ($SiMe_4$) 7.74, 7.74, and 7.71 (3 × 2 H, galloyl), 7.69 and 7.43 (2 × 1 H, hexahydroxydiphenoyl), 6.21 (d, *J* 2.5 Hz, glucose 1-H, 5.42 (dd, *J* 2.5, 7.0 Hz, glucose 2-H), 5.84 (t, *J* 7.0 Hz, glucose 3-H), 5.06 (dd, *J* 2.0, 7.0 Hz, glucose 4-H), 4.80 (dd, *J* 2.0, 11.0, glucose, 6-H), 4.65 (m, *J* 2.0, 2.0, 4.0, and 11.0 Hz, glucose 5-H), and 4.50 (dd, *J* 4.0, 11.0 Hz, glucose 6-H.)

β-1,6-(S)-*Hexahydroxydiphenoyl*-2,4-*dehydrohexahydroxydiphenoyl*-D-*glucopyranose* (9).—The phenolic ester was isolated from leaves of *Punica granatum* and *Davidia involucrata* as a yellow powder by repeated evaporation from anhydrous acetone (Found: C, 50.5; H, 3.5. $C_{34}H_{22}O_{22}\cdot H_2O$ requires C, 51.0; H, 3.0%), $[\alpha]_D^{20}$ +9.5° (*c* 0.5, MeOH); R_F(A) 0.42; R_F(B) 0.17; ^1H n.m.r. ([$^2H_6$]acetone, 24 h) δ ($SiMe_4$) 6.85, 6.79, 6.84, and 6.80 (hexahydroxydiphenoyl); ^{13}C n.m.r. ([$^2H_6$]acetone/$SiMe_4$) δ values after 24 h 194.6 and 192.0 (CO), 168.2, 166.2, 165.6, and 165.3 (aroyl ester CO), 138.7, 136.9, and 136.3 (C-4 hexahydroxydiphenoyl), 96.0, 92.5; 89.9 (C-1), and 70.9, 69.3, 64.1, 61.9, and 60.9 (glucose C), 51.8, and 45.9 p.p.m.

The *phenazine derivative* (15) was prepared analogously to the phenazine derivatives of geraniin, isogeraniin, and granatin B (see above). The compound separated from solution during preparation and was recrystallised from acetonitrile as pale yellow needles, m.p. >300 °C (Found: C, 52.2; H, 3.5; N, 2.7. $C_{40}H_{26}N_2O_{20}\cdot 3H_2O$ requires C, 52.3; H, 3.5; N, 3.1%), $[\alpha]_D^{20}$ +93° (*c* 0.6, acetone); ^{13}C n.m.r. [$(CD_3)_2SO$/$SiMe_4$] δ values after 1 h 167.9, 165.6, 165.3, and 165.0 (aroyl ester CO), 138.0, 135.8, 135.1, and 134.6 (C-4 hexahydroxydiphenoyl), 88.8, 72.9, 69.9, 68.7, 63.1, and 58.7 p.p.m. (glucose C), ([$^2H_5$]pyridine/$SiMe_4$); δ values after 24 h 169.5, 168.1, 167.3, and 166.7 (aroyl ester CO), 138.6, 137.4, 136.3, and 135.3 (C-4 hexahydroxydiphenoyl groups), and 90.6, 74.3 (2×), 71.5, 64.6, and 60.7 p.p.m. (glucose C).

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