245. Studies on Monoterpene Glucosides and Related Natural Products

Part 51[1])

Absolute Structures of Hydrangenosides A, B, C, D, E, F, and G. Novel Type Secoiridoid Glucosides from Two *Hydrangea* Plants[2])

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Summary

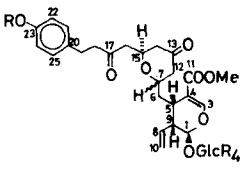
From *Hydrangea macrophylla* var. *macrophylla,* four new secoiridoid glucosides, hydrangenosides A, B, C and D, were isolated, along with the known iridoid glucosides loganin, secologanin, secologanic acid and sweroside. Moreover, hydrangenosides E, F, and G, the glucosides of the same class, were isolated together with hydrangenosides C and D from *Hydrangea scandens*. Based on spectroscopic and chemical methods, the novel structures of the new glucosides consisting of secologanin and a shikimate-malonate-derived unit which are joined by a C–C bond were elucidated. However, seven other *Hydrangea* plants were tested and found not to contain hydrangenoside-type glucosides.

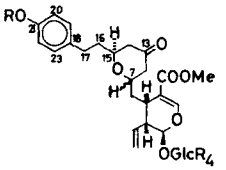
In 1964, *Plouvier* reported the isolation of loganin (**10**) from *Hydrangea aspera* D. DON, *H. bretschneideri* DIPP., and *H. xanthoneura* DIELS. [5]. However, no other study has been recorded on iridoid constituents of *Hydrangea* species *(Saxifragaceae)* since then. We thus examined glucoside constituents of *H. macrophylla* (THUNB.) Ser. var. *macrophylla,* which is known to contain hydrangenol (**8**) [6] and hydrangenol glucoside (**9**) [7], and isolated four new secoiridoid glucosides, hydrangenosides A (**1**), B (**2**), C (**3**), and D (**4**) along with the known iridoid glucosides. In addition to these, hydrangenosides E (**5**), F (**6**), and G (**7**) of the same type of secoiridoid glucosides were isolated together with hydrangenosides C (**3**) and D (**4**) from the congeneric plant, *Hydrangea scandens* (LINN. fil.) SERINGE. We have established that the seven new secoiridoid glucosides have novel structures consisting of secologanin (**11**) and a shikimate-malonate-derived unit, which are joined by a C–C bond. This paper deals with the structure elucidation of these glucosides.

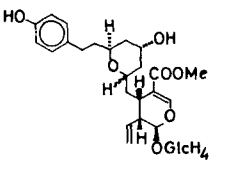
[1]) For Part 50, see [1].

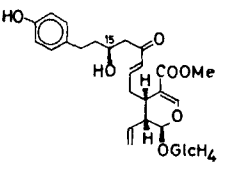
[2]) For preliminary reports of this work, see [2–4].

The overground parts of *H. macrophylla* var. *macrophylla* were extracted with hot H_2O, and the extract was treated with AcOEt. On concentration, AcOEt layer deposited hydrangenol glucoside (**9**). After removal of **9**, the filtrate was further concentrated and fractionated by a combination of silica gel column chromatography, droplet counter current chromatography, preparative TLC, and HPLC giving hydrangenosides A (**1**), B (**2**), C (**3**), and D (**4**). On the other hand, a BuOH-soluble portion of the remaining H_2O layer was also fractionated by several chromatographies on polyamide, charcoal, and silica gel affording loganin (**10**), secologanin (**11**) [8], secologanic acid (**12**) [9], and sweroside (**13**) [10].









7 Hydrangenoside G

1[3]) R=H, 7⟶H, Hydrangenoside A

2 R=H, 7⋯H, Hydrangenoside B

14 R=Ac, 7⟶H

34 R=Ac, 7⋯H

3 R=H, 7⟶H, Hydrangenoside C

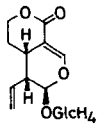
4 R=H, 7⋯H, Hydrangenoside D

40 R=Ac, 7⟶H

41 R=Ac, 7⋯H

5 7⋯H, Hydrangenoside E

6 7⟶H, Hydrangenoside F



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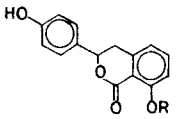
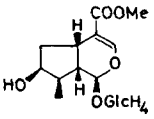
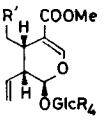






8 R=H

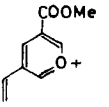
9 R=GlcH$_4$

10

11 R=H, R′=CHO

12 R=H, R′=COOH

16 R=Ac, R′=CHO



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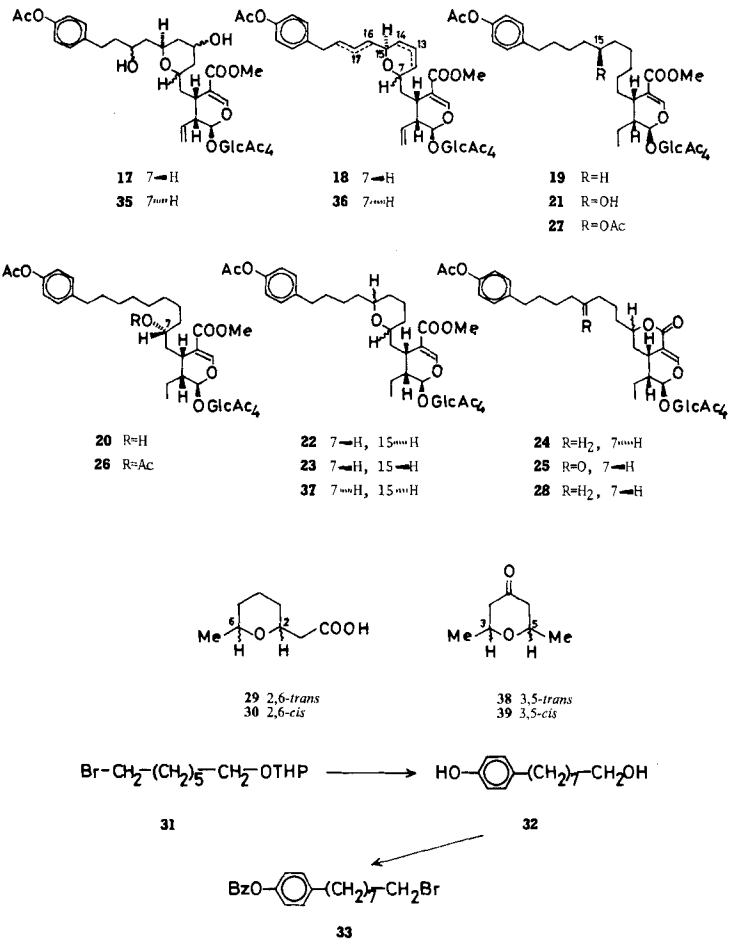
Hydrangenoside A (**1**)[3]), $C_{31}H_{40}O_{13} \cdot \frac{1}{2}\ H_2O$, $[\alpha]_D = -85.2°$ (MeOH), was obtained as a white powder. Its formula was confirmed by fast-atom-bombardment (FAB) MS (*m/z* 621 ($(M + H)^+$), 643 ($(M + Na)^+$)). The spectral data (UV, IR, ^{1}H- and ^{13}C-NMR) of hydrangenoside A (**1**) and its acetate **14** led us to presume that the new glucoside possesses structure **1** consisting of a (*p*-hydroxyphenyl)ethylcarbonyl group and secologanin (**11**) [2]. In fact, electron-impact (EI) MS of **14** showed a peak at *m/z* 165 (**15**) [11] characteristic of secoiridoid glucosides such as secologanin (**11**) and secologanic acid (**12**).

The presumed structure **1** was verified by chemical degradations as follows. $NaBH_4$ reduction of its acetate **14** in THF furnished a diol **17**, which on mesylation followed by 2,6-dimethylpyridine-induced elimination of MsOH yielded olefin **18**. This compound was hydrogenated over 10% Pd/C in AcOH at 60° resulting in the formation of the following seven reduction products: **19** (7.4% yield), **20** (8.4%), **21** (3.7%), **22**

[3]) The indicated numbering in the formulae is arbitrary. The systematic numbering is used in the systematic names in the *Exper. Part.*



(25.2%), **23** (10.3%), **24** (6.2%), and **25** (8.8%). The structures of all these degradation products were supported by their spectroscopic properties and further chemical transformation (acetylation of **20** and **21** (→**26**, **27**); lactonization of **20** (→**28**); synthesis of **24** and **28**).

Compound **19**, $C_{41}H_{58}O_{15}$, showed signals for 9 CH_2-groups at δ 1.24 and a COOMe-group at δ 3.66 in the ^{1}H-NMR spectrum. Opening of the dihydropyran ring of **18** accompanied by removal of the resultant OH-group and subsequent reduction of double bonds might be its way of formation.

Both compounds **20** and **21**, each having $C_{41}H_{58}O_{16} \cdot H_2O$, showed ^{1}H-NMR signals for a $PhCH_2$-group (δ 2.58), a COOMe-group (δ 3.74 in **20** and 3.68 in **21**), and 9 CH_2-groups (δ 1.10–1.80). The ^{13}C-NMR spectra of **20** and **21** were very similar except that a OH-bearing methine C-atom of **20** resonated upfield (δ 67.5) relative to that (δ 71.6) of **21**, whereas *C*(11)OOMe of **20** appeared downfield (δ 169.4) relative to that (δ 167.8) of **21**. The above spectral difference can be interpreted in terms of H-bonding [12] between 7-OH and C(11)OOMe in **20**, but not between the corresponding groups in **21**. Additionally, on acetylation **20** and **21** gave hexaacetates **26** and **27**, respectively. From the evidence mentioned so far, **20** and **21** should be 7-OH- and 15-OH-substituted, respectively. This was also supported by the formation of lactone **28** from **20** through mesylation and concomitant H_2O-*mediated lactonization*.

Both compounds **22** and **23**, each having $C_{41}H_{56}O_{16}$, showed ^{1}H-NMR signals for 8 CH_2-groups (δ 1.10–1.80), a COOMe-group (δ 3.68 in **22** and 3.65 in **23**), and H–C(7) and H–C(15) of the tetrahydropyran ring (δ 3.72 in **22** and 3.20 in **23**). The observed difference in chemical shifts of H–C(7) and H–C(15) of **22** and **23** can be explained in the following way. The tetrahydropyran ring of **22** with *trans*-configuration at C(7) and C(15) exists in two rapidly equilibrating chair conformations, thus permitting H–C(7) and H–C(15) to show an ax/eq time-averaged signal in the ^{1}H-NMR spectrum. In contrast, the tetrahydropyran ring of **23** having a stable *cis*-configuration with two diequatorial substituents steers H–C(7) and H–C(15) to assume axial positions. Accordingly, both H–C(7) and H–C(15) of **22** resonate at a lower field than those of **23**. Comparison of the ^{13}C-NMR spectra of **22** and **23** with those of (*trans*-6-methyltetrahydropyran-2-yl)acetic acid (**29**) and its *cis*-isomer **30** [13] supported the *cis*/*trans*-assignments. Compound **23** is considered to be a by-product formed by isomerization concomitant with the catalytic reduction of **18** which will be discussed later.

Compound **24**, $C_{40}H_{54}O_{15}$, had a ^{1}H-NMR spectrum similar to that of **20**. However, **24** showed no COOMe-signal, but a signal due to an acyloxy-bearing CH at δ 4.30–4.60 in place of the OH-bearing CH of **20** (δ 3.32). Thus, **24** was presumed to be a lactone which would be formed from **20**.

Compound **25**, $C_{40}H_{52}O_{16}$, did not show the singlet of the COOMe-group in the ^{1}H-NMR spectrum; it showed ^{13}C-NMR signals due to a keto-CO at δ 210.2 and the 2 CH_2 linked to it at δ 42.1 and 42.4. Thus, **25** was presumed to be a lactone comprising a C(15)=O group, formed on catalytic reduction of **18** by migration of a double bond from the 13,14- or 16,17- to the 14,15- or 15,16-position and subsequent attack of the C(11)OOMe O-atom at C(7) resulting in the cleavage of C(7)–O bond.

Next, to confirm the presumed structures of lactones **24** and **28**, their syntheses were carried out in the following way [2]. The 7-bromohept-1-yl tetrahydropyran-2-yl ether (**31**) [14] was converted, *via* 8-(*p*-hydroxyphenyl)octan-1-ol (**32**), to 8-(*p*-benzyloxyphenyl)octyl bromide (**33**). This compound was condensed with secologanin tetraacetate (**16**) by a *Grignard* reaction. The condensation product was hydrogenated and acetylated to yield a pair of lactones in a ratio of 1:4, of which the minor product was identical with **24** obtained in the hydrogenation of olefin **18**, whereas the major one was identical with **28** derived from 7-alcohol **20**. Furthermore, the presence of a nuclear *Overhauser* effect (NOE) between H–C(5) (δ 2.70–3.03, *m*) and H–C(7) (δ 4.20–4.80, *m*) of **28** (absent in **24**) demonstrated (*S*)- and (*R*)-chirality for C(7) in **28** and **24**, respectively.

Since the conversion of acetate **14** *via* **18** into lactone **24** is expected to occur with retention of the configuration at all asymmetric centers except for C(15), the absolute configuration of **14** and hence, that of hydrangenoside A (**1**) was established (the C(15) configuration will be discussed below).

Hydrangenoside B (**2**), $C_{31}H_{40}O_{13}\cdot H_2O$, $[\alpha]_D = -80.9°$ (MeOH), was obtained as a white powder. It was presumed to be a C(7) and/or C(15) stereoisomer of hydrangenoside A (**1**) based on the spectral comparison of these two compounds [3]. Thus, the pentaacetate **34** of **2** was subjected to the same chemical modification as was **14**, leading to the tetrahydropyran **37** (37.7% yield), the 15-alcohol **21** (7.5%), and the (7*S*)-lactone **28** (9.5%) *via* diol **35** and olefin **36**.

Compound **37**, $C_{41}H_{56}O_{16}$, showed the ^{1}H- and ^{13}C-NMR spectra similar to those of *cis*-tetrahydropyran **23** derived from hydrangenoside A pentaacetate (**14**), especially in terms of the chemical shifts of H–C(7) and H–C(15) (centered at δ 3.20) and C(7) and C(15) (δ 75.6 and 77.7). Therefore, **37** was presumed to be another *cis*-tetrahydropyran having the C(7) and C(15) configurations opposite to those of **23**. Especially the formation of (7*S*)-lactone **28** from **34** clarified the structure of hydrangenoside B (**2**), except for the C(15) configuration. This remaining problem, concerning hydrangenosides A (**1**) as well, was solved by ^{13}C- and ^{1}H-NMR analyses.

In the ^{1}H-NMR spectrum, H–C(7) and H–C(15) of hydrangenoside B pentaacetate (**34**) resonated upfield (δ 3.75 and 4.05) as compared with the corresponding protons (δ 4.20 and 4.60) of hydrangenoside A pentaacetate (**14**). Furthermore, in the ^{13}C-NMR spectrum, both C(15) and C(7) of **34** resonated downfield by 1.8–4.2 ppm relative to the corresponding C-atoms of **14**. These observations can reasonably be explained by the following: *i*) the *trans*-oriented H–C(7) and H–C(15) of **14** resonate at lower field than the *cis*-oriented of **34**, as it was observed for the corresponding H-signals of *trans*- and *cis*-tetrahydropyrans **22** and **23**, respectively.

ii) Two pairs of protons, H–C(7)/H–C(16) and H–C(6)/H–C(15), in **14** are *cis*-oriented and are in close proximity. Therefore, the signals of the C-atoms bearing these protons show upfield shifts due to the reciprocal γ-effect. Contrastingly, the corresponding two pairs of protons of **34** are *trans* and are free from the steric compression. Thus, the signals of the concerned C-atoms appear at lower field.

The NMR-deduced configuration at C(15) received support from the following facts: *i*) the above NMR-spectral correlation was consistent with that of two model compounds, *trans*-3,5-dimethyl-4-oxacyclohexanone (**38**) and its *cis*-isomer **39** [15]. *ii*) The above described chemical conversion of **34** yielded only the *cis*-configurated tetrahydropyran **37**, whereas **14** afforded both *cis*- and *trans*-isomers **23** and **22**, respectively. This difference is probably due to the different configuration of the tetrahydropyran moiety of **34** and **14**. The more stable *cis*-configuration of **34** with the C(7) and C(15) substituents in diequatorial position was retained during the transformation **34**→→**37**, whereas compound **14** with the less stable *trans*-configuration underwent isomerization on the stage of the olefinic intermediate **18**, caused by migration of a double bond from the 13,14- or 16,17- to the 14,15- or 15,16-position and subsequent hydrogenation [16].

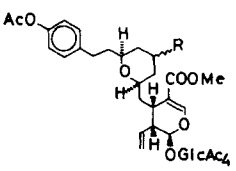
From the evidence obtained so far, it was concluded that the orientation of the C(7) and C(15) substituents of **14** and **34** are *trans* and *cis*, respectively. Since the respective C(7) configurations of **14** and **34** are (*S*) and (*R*) *(vide supra)*, the C(15) of both compounds should be (*S*)-configurated. Therefore, the absolute configuration of **14** and **34**, and hence, those of hydrangenosides A (**1**) and B (**2**) were established.

Hydrangenoside C (**3**), $C_{29}H_{38}O_{12}\cdot H_2O$, $[\alpha]_D = -94.7°$ (MeOH), was obtained as a white powder, whereas hydrangenoside D (**4**), $C_{29}H_{38}O_{12}\cdot H_2O$, $[\alpha]_D = -126.3°$ (MeOH), as colourless needles, m.p. 186–187°. The spectral comparison of **3**, **4** and their derivatives with hydrangenosides A (**1**), B (**2**) and their derivatives led to a presumption that hydrangenosides C and D have structures **3** and **4**, respectively, each comprising one acetate unit fewer than **1** and **2** [3]. Catalytic reduction of hydrangenoside C pentaacetate (**40**) and hydrangenoside D pentaacetate (**41**) and further conversions of the resulting products were the same as in the cases of **14** and **34**, confirming the presumed structures.

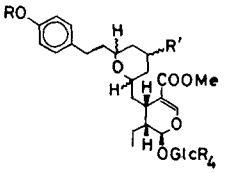
The isolation of the above described novel type secoiridoid glucosides prompted us to examine other *Hydrangea* plants: *H. macrophylla* (THUNB.) Ser. var. *megacarpa* OHWI, *H. macrophylla* (THUNB.) Ser. var. *thunbergii* (SIEBOLD) MAKINO, *H. macrophylla* (THUNB.) Ser. var. *acuminata* (SIEB. et ZUCC.) MAKINO, *H. scandens* (LINN. *fil.*) SERINGE, *H. paniculata* SIEBOLD, *H. petiolaris* SIEB. et ZUCC., *H. luteo-venosa* KOIDZ, and *H. hirta* (THUNB.) SIEBOLD. The residue of the MeOH extract of each plant was taken up in H_2O and the solution was further treated with BuOH. The BuOH-soluble portion was fractionated into glucoside fractions by repeated silica gel column chromatography. Among the above plants, some of which were found to contain usual iridoid series glucosides[4]), only *H. scandens* gave new type glucosides, *i.e.* hydrangenosides C (**3**), D (**4**), E (**5**), F (**6**), and G (**7**).

Hydrangenoside E (**5**), $C_{29}H_{40}O_{12}\cdot H_2O$, $[\alpha]_D = -108.7°$ (MeOH), was obtained as a white powder. This compound was presumed to be a 13-OH congener of hydrangenoside D (**4**) by spectral comparison of **5** and its acetate **42** with **4** and its pentaacetate **41**

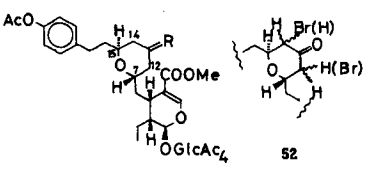
[4]) The occurrence of these glucosides in the *Hydrangea* plants will be reported elsewhere.



42 R=⋯OAc
43 R=⋯OH
44 R=⇢OH
45 R=⇢OAc



46 R=Ac, R′=⋯OH, 7⇢H, 15⋯H
47 R=Ac, R′=⇢OH, 7⇢H, 15⋯H
48 R=Ac, R′=⋯OAc, 7⇢H, 15⋯H
49 R=Ac, R′=⇢OAc, 7⇢H, 15⋯H
50 R=H, R′=⋯OH, 7⇢H, 15⋯H
56 R=Ac, R′=⋯OH, 7⇢H, 15⇢H
57 R=Ac, R′=⇢OH, 7⋯H, 15⋯H



51 R=O
53 R=O, 7,12-dehydro
54 R=O, 14,15-dehydro
55 R= , 14,15-dehydro

52

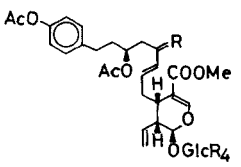
[4]. Thus, the acetate **41** of **4** was reduced with $NaBH_4$ to give a pair of 13-epimeric alcohols **43** and **44** in a ratio of 1:8, which on acetylation yielded the corresponding acetates **42** and **45**. Of these acetates, the minor product **42** was identical with the hexaacetate of hydrangenoside E (**5**). The C(13) configuration was determined by comparison of the ^{13}C-NMR spectra of **43** and **44** [4].

Hydrangenoside F (**6**), $C_{29}H_{40}O_{12} \cdot 2H_2O$, $[\alpha]_D = -87.0°$ (MeOH), was obtained as a white powder. It was assumed to be a 13-OH congener of hydrangenoside C (**3**) based on the spectral evidence [4]. Thus, pentaacetate **40** of hydrangenoside C (**3**) was converted, by $NaBH_4$ reduction followed by Pd/C-catalyzed hydrogenation, into the 13-epimeric alcohols **46** and **47** (ratios of 5:2). On acetylation, they afforded the acetates **48** and **49**, respectively. The major one, **48**, was identical with the hexaacetate of dihydrohydrangenoside F (**50**), which was obtained by Pd/C-catalyzed reduction of hydrangenoside F (**6**).

Based on these results, the absolute configuration of hydrangenoside F (**6**) was established, with the only ambiguity being an uncertainty regarding the C(13) configuration. This problem was solved in the following way. Catalytic reduction of hydrangenoside C pentaacetate (**40**) gave the dihydro compound **51**, which on treatment with Br_2 yielded a mixture **52** ($C_{39}H_{47}BrO_{17}$); in its ^{13}C-NMR spectrum, two sets of signals appeared arising from CHBr- (δ 52.9, 54.9, 55.9, and 56.5) and CH_2-groups (δ 42.0, 44.1, 44.4, and 44.9), all linked to the 13-oxo group. This unequivocally indicated that **52** is a mixture of 4 isomers substituted by Br at C(12) and C(14). Dehydrobromination of **52** with MgO yielded two olefins **53** and **54** in a ratio of 1:3. For both compounds (each having $C_{39}H_{46}O_{17}$), the ^{13}C-NMR spectra showed the olefinic C-atoms to be conjugated with the C(13)=O (δ 105.7 (*d*) and 175.2 (*s*) in **53**; δ 104.6 (*d*) and 176.3 (*s*) in **54**). These data indicated that **53** and **54** are positional isomers with respect to the double bond conjugated to C(13)=O. The major product **54** was reduced with $NaBH_4$ in MeOH at 0–5° to yield 13-alcohol **55** as the sole product ($C_{39}H_{50}O_{17}$; IR: 3460 cm^{-1} (OH); ^{13}C-NMR: OH-bearing CH at δ 63.6 (*d*), non-conjugated olefinic C-atoms at δ 101.1 (*d*) and 155.2 (*s*)). Compound **55** was then hydrogenated over Pt to afford a pair of dihydro compounds **46** and **56** in a ratio of 1:15; the 13-acetate of the minor product **46** was identical with the hexaacetate **48** of dihydrohydrangenoside F (**50**). On the other hand, the ^{13}C-NMR spectrum of the major product **56** was very similar to that of dihydro-13-epihydrangenoside E pentaacetate (**57**) obtained by Pd/C-catalyzed reduc-

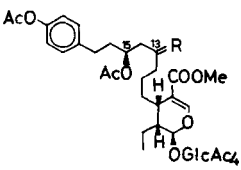
tion of **44**, especially in terms of the C-signals of the tetrahydropyran ring. Thus, it was presumed that the tetrahydropyran moieties of **56** and **57** have the same relative configuration at C(7), C(13) and C(15), but are antipodal to each other. Accordingly, C(13) of **56** should have the (*S*)-configuration, being opposite to that of **44** and **57**. Since **46** should possess the same chirality at C(13) as does **56**, both **50** and **48** and hence, hydrangenoside F (**6**) were concluded to have the (*S*)-configuration at C(13).

It should be noted that the two catalytic-reduction products of **55** have identical configuration at C(7). This fact strongly suggests that **53** has the double bond at the 7,12-position, whereas **54** has it at the 14,15-position.



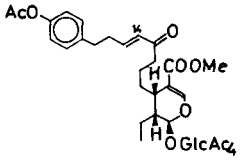
58 R=O

59 R=OH, H



60 R=H_2

61 R=O



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Hydrangenoside G (**7**), $C_{29}H_{38}O_{12} \cdot H_2O$, $[\alpha]_D = -104.1°$ (MeOH), was obtained as a white powder. The spectral evidence, as well as biogenetic consideration of hydrangenoside series glucosides, led to a presumption that hydrangenoside G[5]) has the structure **7** [4]. This was verified by chemical modifications: $NaBH_4$ reduction of hydrangenoside G hexaacetate (**58**) afforded a mixture **59** of two isomeric alcohols, which on Pd/C catalyzed reduction yielded the 15-acetoxy compound **60** as the sole product. This was identical with the acetate of (15*R*)-alcohol [3] derived from hydrangenoside C pentaacetate (**40**). Furthermore, catalytic reduction of **58** over Pd/C yielded the tetrahydro compound **61**, which on treatment with alumina afforded another conjugated ketone **62**. Thus, the OH- and keto groups in **7** were accomodated to the (*S*)-configurated C(15) and the C(13), respectively.

We express our sincere gratitude to Prof. *emer. D. Satoh* (Tokushima Bunri University) for encouragements and to Dr. *S. Imai (Takeda Pharmaceutical Industries Co., Ltd.)* for extraction of the plant material. We are also grateful to Prof. *T. Shingu* (Kobe-Gakuin University) and Drs. *K. Kitamura* (Kyoto College of Pharmacy), *K. Kida* (Tokushima University) and *Y. Kuroda* (this University) for NMR spectra, to Mr. *N. Nojima (Jeol Ltd.)* and Mrs. *N. Tokunaga* (T.B.U.) for mass spectra and to the staff of the Microanalytical Centre (this University) and Misses *M. Oe* (T.U.) and *Y. Onishi* (T.B.U.) for elemental analyses.

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[5]) At first, the name, hydrangenoside G, was given to hydrangenoside F dimethylacetal (*S. Uesato, T. Hashimoto, K. Uobe, Y. Takeda, H. Inouye, H. Taguchi & T. Endo,* Tennen Yuki Kagobutsu Toronkai Koen Yoshishu, 24th, 1981, 9 (Japan); Chem. Abstr. 96, 177923n (1982)). However, since this compound was found to be an artefact formed from hydrangenoside F during isolation, compound **7** was hereafter referred to as hydrangenoside G.

Experimental Part

1. *General.* Melting points were determined on a *Yanagimonto* micromelting point apparatus and are uncorrected. Optical rotations were masured with a *Jasco-DIP-180* automatic digital polarimeter. UV spectra were recorded on a *Hitachi-EPS-3* or model *200-20* spectrophotometer in MeOH (λ_{max} in nm, log ε in parenthesis) and IR spectra on a *Hitachi-EPI-S* spectrometer or a *Shimadzu-IR-27G* grating infrared spectrometer (absorption maxima in cm^{-1}). ^{1}H-NMR spectra were recorded on *Varian-HA-100* spectrometer of *Jeol-JMN-PS-100* spectrometer, while ^{13}C-NMR spectra on *Hitachi-R-42-FT-NMR* (22.6 MHz) or *Jeol-JNM-FX-100-FT-NMR* (25.0 Hz) spectrometer using CD_3OD and $CDCl_3$ for free glucosides and other compounds, respectively. Chemical shifts are given in ppm relative to TMS as internal reference, coupling constants (J) are reported in Hz; s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet. EI-MS were obtained with a *Shimadzu-LKB-9000B* GC-MS spectrometer with a *GC-MS PAC-500* data system at 70 eV ionizing electron energy, source temperature 270°. FAB-MS were recorded on a *Jeol-JMS-D-300* spectrometer with a *SS-200* data system. The target was bombarded with 3.0 KeV Xe-atoms, the ion source was at 230°/1×10^{-7} Torr. Important peaks in m/z. Silica gel *AR-100 (Mallinckrodt)*, silica gel 60 *(Merck)*, activated charcoal *(Wako)*, polyamide (*Wako* and *Ube Kosan*) were employed for gravity-column chromatography. Silica gel PF_{254} *(Merck)* was used for medium-pressure column chromatography. TLC was carried out on silica gel 60 GF_{254} or 'DC-Alufolien' silica gel *60* F_{254} *(Merck)* and prep. TLC on silica gel *60* PF_{254}, silica gel PF_{254} or 'DC-Fertigplatten' silica gel F_{254}; detection by UV irradiation or by I_2 vapour. Bands were scraped off and extracted with $CHCl_3$/MeOH 9:1, and extracts were concentrated *in vacuo*. Ratios of solvents are expressed in vol-%. $MgSO_4$ was used as a drying reagent for solvents. Acetylation was carried out using Ac_2O/pyridine by the conventional manner.

2. *Isolation of Glucosides from* Hydrangea macrophylla *Ser. var.* macrophylla. Fresh leaves and twigs of *H. macrophylla* (137 kg) collected at Aioi-cho (Tokushima Pref.) in August 1979 were steamed at 98° for 10 min and extracted with H_2O (3 × 250 l) at 60° for 1 h. The combined extracts were concentrated *in vacuo* to 73 l and treated with AcOEt (3 × 43 l). The aq. layer was separated and further partitioned with BuOH (4 × 220 l), and an aliquot (12 g) of BuOH-soluble portion (180 g) was chromatographed on polyamide (300 g) with H_2O (1 l) to yield a glucoside fraction (6.7 g). This was chromatographed on a charcoal (500 g) column with H_2O/MeOH with increasing MeOH contents. The residue (5.0 g) of the eluate with 50–100% MeOH was chromatographed on silica gel (120 g) and eluted with MeOH/$CHCl_3$ with increasing MeOH contents. The 1–2, 3–5, and 7% MeOH/$CHCl_3$ eluents gave residues, *Chrom-1* (0.67 g), *Chrom-2* (2.50 g) and *Chrom-3* (0.5 g), respectively. *Chrom-1* was subjected to prep. TLC ($CHCl_3$/MeOH 85:15, 5 developments) to give secologanic acid (**12**; 9 mg). *Chrom-2* was subjected to prep. TLC ($CHCl_3$/MeOH 8:2) to yield secologanin (**11**; 2.10 g) as a white powder. An aliquot (0.20 g) of **11** was acetylated and the product purified by prep. TLC (benzene/hexane/MeOH 4.5:4.5:1) followed by recrystallization from EtOH/hexane to furnish secologanin tetraacetate (**16**) as colourless needles, m.p. 113.5°. *Chrom-3* was subjected to prep. TLC ($CHCl_3$/MeOH 9:1) yielding sweroside (**13**; 3 mg) and loganin (**10**; 9 mg), both as a white powder. On acetylation, **13** afforded the tetraacetate as colourless needles, m.p. 167–168°, whereas **10** gave the pentaacetate as colourless needles, m.p. 138–140°.

The AcOEt solution, after separating the aq. layer, was allowed to stand overnight at r.t., and the resulting precipitate was filtered off and recrystallized from AcOEt to yield hydrangenol glucoside (**9**; 481 g) as colourless needles, m.p. 189–191°. The filtrate was concentrated *in vacuo* to give a residue (584 g), an aliquot (117 g) of which was chromatographed on a silica-gel (1400 g) column with MeOH/$CHCl_3$ with increasing MeOH contents. A 5-l fraction for each 1% of MeOH raise was collected. The eluate with 10% MeOH/$CHCl_3$ afforded a glucoside fraction (14.0 g), an aliquot (1.5 g) of which was subjected to droplet counter-current chromatography (DCCC; 100 glass tubes, 2.4 mm i.d. × 140 cm, *Teflon* tubes, 1.4 mm i.d. × 140 cm; solvent: $CHCl_3$/benzene/MeOH/H_2O 15:15:23:7, descending method); collecting 7-ml fractions. The residue (43 mg) of *Fractions 421–470* was subjected to prep. TLC ($CHCl_3$/MeOH 5:1, 2 developments). The main band gave a crystalline compound (18 mg), which was recrystallized from acetone to furnish hydrangenoside D (**4**; 9 mg) as colourless needles, m.p. 186–187°. The residue (412 mg) of *Fractions 471–610* was subjected to HPLC (*Bondapak* C_{18}; column size, 7.8 × 30 cm; 50% MeOH, flow rate 2.0 ml/min) to furnish hydrangenoside A (**1**) (137 mg), B (**2**) (27 mg) and C (**3**) (82 mg). The residue (454 mg) of *Fractions 611–730* was found to be pure hydrangenoside A (**1**).

Hydrangenoside A (= *Methyl 3α-Ethenyl-2β-(β-*D*-glucopyranosyloxy)-3,4-dihydro-4α-{[3,4,5,6-tetrahydro-6β-[4-(*p*-hydroxyphenyl)-2-oxobutyl]-4-oxo-2*H*-pyran-2α-yl]methyl}-2*H*-pyran-5-carboxylate;* **1**). White powder; $[\alpha]_D^{29} = -85.2°$ (c = 1.00, MeOH). UV: 226.0 (4.10), 238.0 (sh, 4.04), 276.0 (sh, 2.82). IR: 3400, 1710, 1630, 1600, 1520, 1070. ^{1}H-NMR: 2.10–3.00 (*m*, CH_2(12), CH_2(14), CH_2(16)); 2.80 (br. *s*, CH_2(18), CH_2(19)); 3.68 (*s*, $COOCH_3$); 6.62–7.10 (*AA'BB'*, 4 arom. H); 7.47 (*s*, H–C(3)). ^{13}C-NMR: 29.6 (*d*, C(5); *t*, C(19)); 35.9 (*t*, C(6));

45.2 (*d*, C(9)); 46.1, 46.9, 47.1, 48.0 (4*t*, C(12), C(14), C(16), C(18)); 51.8 (*q*, $COOCH_3$); 69.5, 72.2 (2*d*, C(7), C(15)); 97.5, 99.8 (2*d*, C(1), anom. C); 111.7 (*s*, C(4)), 116.1 (*d*, C(22), C(24)); 119.9 (*t*, C(10)); 130.2 (*d*, C(21), C(25)); 133.0 (*s*, C(20)); 135.4 (*d*, C(8)), 153.6 (*d*, C(3)); 156.2 (*s*, C(23)); 168.9 (*s*, C(11)); 209.5, 210.0 (2*s*, C(13), C(17)). MS (FAB): 643 ($(M + Na)^+$), 621 ($(M + 1)^+$), 459 ($[(M + 1) - 162]^+$), 441 ($[(M + 1) - 180]^+$). Anal. calc. for $C_{31}H_{40}O_{13} \cdot \frac{1}{2}H_2O$: C 59.13, H 6.56; found: C 59.53, H 6.71.

Hydrangenoside B (= *7-Epihydrangenoside A;* **2**). White powder, $[\alpha]_D^{25} = -80.0°$ (c = 0.85, MeOH). UV: 227.5 (4.20), 279.0 (3.29). IR: 3400, 2930, 1710, 1695, 1630, 1600, 1520, 1070, 1040. ^{1}H-NMR: 1.72 (*m*, CH_2(6)); 2.78 (br. *s*, CH_2(18), CH_2(19)); 3.67 (*s*, $COOCH_3$); 6.68–7.01 (*AA'BB'*, 4 arom. H); 7.44 (*s*, H–C(3)). MS (FAB): 643 ($(M + Na)^+$), 621 ($(M + 1)^+$), 459 ($[(M + 1) - 162]^+$), 441 ($[(M + 1) - 180]^+$). Anal. calc. for $C_{31}H_{40}O_{13} \cdot H_2O$: C 58.30, H 6.63; found: C 58.42, H 6.67.

Hydrangenoside C (= *Methyl 3α-Ethenyl-2β-(β-*D*-glucopyranosyloxy)-3,4-dihydro-4α-{[3,4,5,6-tetrahydro-6β-[2-(*p*-hydroxyphenyl)ethyl]-4-oxo-2*H*-pyran-2α-yl]methyl}-2*H*-pyran-5-carboxylate;* **3**). White powder, $[\alpha]_D^{25} = -94.7°$ (*c* = 1.12, MeOH). UV: 227.0 (4.21), 280.0 (3.24). IR: 3400, 1710, 1690, 1630, 1515, 1290, 1080, 1040. ^{1}H-NMR: 1.78 (*m*, CH_2(6)); 3.68 (*s*, $COOCH_3$); 6.73–7.07 (*AA'BB'*, 4 arom. H); 7.47 (*s*, H–C(3)). MS (FAB): 601 ($(M + Na)^+$), 579 ($(M + 1)^+$), 417 ($[(M + 1) - 162]^+$), 399 ($[(M + 1) - 180]^+$), 165 (**15**). Anal. calc. for $C_{29}H_{38}O_{12} \cdot H_2O$: C 58.38, H 6.76; found: C 58.38, H 6.64.

Hydrangenoside D (= *7-Epihydrangenoside C;* **4**). Colourless needles, m.p. 186–187°, $[\alpha]_D^{25} = -126.3°$ (*c* = 1.05, MeOH). UV: 227.0 (4.27), 278.0 (3.22). IR: 3520, 3420, 1690, 1635, 1515, 1290, 1075, 1035. ^{1}H-NMR: 2.70 (*m*, CH_2(12), CH_2(14)); 3.68 (*s*, $COOCH_3$); 5.33 (*d*, *J* = 1.5, H–C(1)); 6.75–7.08 (*AA'BB'*, 4 arom. H); 7.47 (*s*, H–C(3)). MS (FAB): 601 ($(M + Na)^+$), 579 ($(M + 1)^+$), 417 ($[(M + 1) - 162]^+$), 399 ($[(M + 1) - 180]^+$), 165 (**15**). Anal. calc. for $C_{29}H_{38}O_{12} \cdot H_2O$: C 58.38, H 6.76; found: C 58.57, H 6.88.

3. *Hydrangenoside A Pentaacetate* (**14**). White powder, $[\alpha]_D^{25} = -79.3°$ (*c* = 1.00, $CHCl_3$). UV: 222.5 (4.01). IR: 1760, 1715, 1635, 1220, 1040. ^{1}H-NMR: 1.72 (br. *t*, *J* = 5.5, CH_2(6)); 1.91–2.05 (4 OAc); 2.27 (*s*, arom. OAc); 2.85 (br. *s*, CH_2(18), CH_2(19)); 3.68 (*s*, $COOCH_3$); 4.20 (*m*, H–C(7)); 4.60 (*m*, H–C(15)); 6.93–7.23 (*AA'BB'*, 4 arom. H); 7.33 (br. *s*, H–C(3)). ^{13}C-NMR: 27.8 (*d*, C(5)); 28.7 (*t*, C(19)); 34.1 (*t*, C(6)); 43.7 (*d*, C(9)); 44.8, 46.0, 46.6, 46.8 (4*t*, C(12), C(14), C(16), C(18)); 51.1 (*q*, $COOCH_3$); 68.6, 71.9 (2*d*, C(7), C(15)); 95.6, 96.0 (2*d*, C(1), anom. C); 111.2 (*s*, C(4)); 120.1 (*t*, C(10)), 121.2 (*d*, C(22), C(24)); 129.0 (*d*, C(21), C(23)); 132.9 (*d*, C(8)), 138.2 (*s*, C(20)); 148.7 (*s*, C(23)); 150.4 (*d*, C(3)); 166.5 (*s*, C(11)); 206.0, 206.3 (2*s*, C(13), C(17)). MS (EI): 331 ($^+$OGlcAc$_4$), 165 (**15**). Anal. calc. for $C_{41}H_{50}O_{18} \cdot \frac{1}{2}H_2O$: C 58.49, H 6.35; found: C 58.53, H 6.36.

4. *Hydrangenoside B Pentaacetate* (**34**). White powder, $[\alpha]_D^{25} = -79.3°$ (*c* = 1.00, $CHCl_3$). UV: 220.0 (4.12). IR: 1760, 1720, 1630, 1220, 1080, 1040. ^{1}H-NMR: 1.36 (*m*, H–C(6)); 1.89–2.02 (4 OAc); 2.27 (*s*, arom. OAc); 2.92 (br. *s*, CH_2(18), CH_2(19)); 3.68 (*s*, $COOCH_3$); 3.75 (*m*, H–C(7)), 4.05 (*m*, H–C(15)), 6.99–7.25 (*AA'BB'*, 4 arom. H); 7.33 (*s*, H–C(3)). ^{13}C-NMR: 26.1 (*d*, C(5)); 28.8 (*t*, C(19)), 34.3 (*t*, C(6)); 42.5 (*d*, C(9)); 45.0, 46.8, 47.8, 48.4 (4*t*, C(12), C(14), C(16), C(18)); 51.0 (*q*, $COOCH_3$); 72.8, 73.7 (2*d*, C(7), C(15)); 95.3, 95.8 (2*d*, C(1), anom. C); 111.0 (*s*, C(4)); 120.1 (*t*, C(10)); 121.2 (*d*, C(22), C(24)); 129.1 (*d*, C(21), C(25)); 132.9 (*d*, C(8)); 138.3 (*s*, C(20)); 148.7 (*s*, C(23)); 150.1 (*d*, C(3)); 166.5 (*s*, C(11)); 205.7, 206.3 (2*s*, C(13), C(17)). Anal. calc. for $C_{41}H_{50}O_{18}$: C 59.27, H 6.07; found: C 59.58, H 6.18.

5. *Diol* **17** (= *Methyl 4α-{[6β-[4-(*p*-Acetoxyphenyl)-2-hydroxybutyl]-3,4,5,6-tetrahydro-4-hydroxy-2*H*-pyran-2α-yl]methyl}-3α-ethenyl-3,4-dihydro-2β-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyloxy)-2*H*-pyran-5-carboxylate*) *and Diol* **35** (= *7-Epi-***17**). A solution of $NaBH_4$ (0.55 g) in H_2O (2 ml) was added dropwise to a stirred solution of **14** (6.04 g) in THF (360 ml) at r.t. After stirring for 70 min, the excess reagent was decomposed by adding AcOH and the mixture was concentrated *in vacuo*. The residue was taken up in $CHCl_3$ and the $CHCl_3$-soluble portion washed successively with 5% HCl, H_2O, 5% $NaHCO_3$, and H_2O, dried, and evaporated to furnish **17** (4.80 g) as a white powder, $[\alpha]_D^{25} = -112.7°$ (*c* = 1.00, $CHCl_3$). UV: 221.0 (4.13), 271.0 (2.91). IR: 3500, 1760, 1710, 1630, 1370, 1220, 1070, 1040. ^{1}H-NMR: 1.95–2.05 (4 OAc); 2.27 (*s*, arom. OAc); 3.72 (*s*, $COOCH_3$); 6.98–7.25 (*AA'BB'*, 4 arom. H); 7.35 (*s*, H–C(3)). Anal. calc. for $C_{41}H_{54}O_{18}$: C 58.99, H 6.52; found: C 58.96, H 6.48.

In the same way, **34** (840 mg) was converted into **35** (835 mg). White powder, $[\alpha]_D^{25} = -83.3°$ (*c* = 1.00, $CHCl_3$). UV: 213.0 (4.04), 219.0 (4.11), 271.0 (2.78). IR: 3480, 1765, 1715, 1510, 1225, 1080, 1040. ^{1}H-NMR: 1.92–1.96 (4 OAc); 2.27 (*s*, arom. OAc); 3.16–3.68 (*m*, H–C(13), H–C(17)); 3.68 (*s*, $COOCH_3$); 6.95–7.20 (*AA'BB'*, 4 arom. H); 7.32 (*s*, H–C(3)). Anal. calc. for $C_{41}H_{54}O_{18}$: C 58.99, H 6.52; found: C 58.86, H 6.59.

6. *Olefin* **18** (= *Methyl 4α-{[6β-[4-(*p*-Acetoxyphenyl)butenyl]dihydro-2*H*-pyran-2α-yl]methyl}-3α-ethenyl-3,4-dihydro-2β-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyloxy)-2*H*-pyran-5-carboxylate*) *and Olefin* **36** (= *7-Epi-***18**). MsCl (2.4 ml) was added to a solution of **17** (4.80 mg) in pyridine (120 ml) under ice cooling, and the whole was allowed to stand overnight at 4°. The mixture was poured onto ice-cold H_2O, allowed to stand for 1 h, and extracted *with* $CHCl_3$. The $CHCl_3$ layer was washed successively with H_2O, 5% HCl, H_2O, 5% $NaHCO_3$, and

H_2O, dried, and concentrated *in vacuo* to give the bis(methanesulfonate) (5.40 g) as a white powder. This compound was dissolved immediately in 2,6-dimethylpyridine (600 ml) and heated at 170° for 4 h under N_2. After removal of the base *in vacuo*, the residue was taken up in $CHCl_3$, and the $CHCl_3$-soluble portion was washed successively with H_2O, 5% HCl, H_2O, 5% $NaHCO_3$, and H_2O, dried, and concentrated *in vacuo*. The residue (3.60 g) was purified by prep. TLC (Et_2O) to furnish **18** (2.88 g) as a white powder, $[\alpha]_D^{25} = -75.7°$ ($c = 1.00$, $CHCl_3$). UV: 210.0 (4.13), 220.0 (4.17). IR: 1760, 1710, 1630, 1370, 1070, 1040. ^{1}H-NMR: 1.93–2.02 (4 OAc); 2.27 (*s*, arom. OAc); 3.68 (*s*, $COOCH_3$); 5.50–5.85 (*m*, 4 olef. H), 6.98–7.23 (*AA'BB'*, 4 arom. H); 7.30 (*s*, H–C(3)). Anal. calc. for $C_{41}H_{50}O_{16}$: C 61.64, H 6.31; found: C 61.72, H 6.48.

In the same way, **35** (835 mg) was converted into **36** (369 mg). White powder, $[\alpha]_D^{26} = -81.4°$ ($c = 0.50$, $CHCl_3$). UV: 213.0 (4.07), 220.5 (4.15), 270.5 (2.95). IR: 1765, 1715, 1630, 1220, 1080, 1040. ^{1}H-NMR: 1.94–2.05 (4 OAc); 2.27 (*s*, arom. OAc); 3.38 (*m*, H–C(7), H–C(15)); 3.67 (*s*, $COOCH_3$); 5.40–5.92 (*m*, 4 olef. H), 6.96–7.20 (*AA'BB'*, 4 arom. H); 7.34 (*s*, H–C(3)). Anal. calc. for $C_{41}H_{50}O_{16}$: C 61.64, H 6.31; found: C 61.86, H 6.48.

7. *Catalytic Reduction of* **18** *and* **36**. Olefin **18** (2.88 g) was hydrogenated over 10% Pd/C (4.68 g) in AcOH (65 ml) at 60° for 1 h. After removal of the catalyst, the filtrate was concentrated *in vacuo*. The residue (2.93 g) was chromatographed on a silica-gel (300 g) column with benzene, 10% Et_2O/benzene, and 20% Et_2O/benzene (each 500 ml, *Fractions 1–3*) and subsequently with 25% Et_2O/benzene, collecting 15-ml fractions (in total 6 l, *Fractions 4–403*). *Fractions 40–60, 109–142,* and *152–171* gave **19** (212 mg), **23** (296 mg), and **20** (241 mg), resp. The residue (1208 mg) of *Fractions 174–253* was subjected to prep. TLC (Et_2O/benzene 1:3, 6 developments). Of 2 major bands, the more mobile one afforded **22** (723 mg) and the less mobile one furnished **24** (178 mg). *Fractions 315–334* and *339–379* afforded **21** (245 mg) and **25** (252 mg), respectively.

Similarly, **36** (369 mg) was hydrogenated over 10% Pd/C. The products were chromatographed by prep. TLC with Et_2O/benzene 1:3 (6 developments) to afford **37** (140 mg), **28** (34 mg), and **21** (28 mg) in the order of increasing polarity.

*Methyl 4α-[10-(*p*-Acetoxyphenyl)decyl]-3α-ethyl-3,4-dihydro-2β-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyloxy)pyran-5-carboxylate* (**19**). Colourless oil, $[\alpha]_D^{25} = -100.0°$ ($c = 0.95$, $CHCl_3$). UV: 220.0 (4.10), 229.5 (4.11). IR: 1760, 1710, 1635, 1370, 1220, 1070, 1040. ^{1}H-NMR: 1.24 (br. *s*, 9 CH_2); 1.99–2.06 (4 OAc); 2.26 (*s*, arom. OAc); 2.56 (*t*, $J = 8.0$, CH_2(19)); 3.66 (*s*, $COOCH_3$); 6.94–7.18 (*AA'BB'*, 4 arom. H); 7.32 (*s*, H–C(3)). MS (EI): 790 (M^+), 331 ($^+$OGlcAc$_4$). Anal. calc. for $C_{41}H_{58}O_{15}$: C 62.26, H 7.39; found: C 62.58, H 7.18.

*Methyl 4α-[(2*R*)-10-(*p*-Acetoxyphenyl)-2-hydroxydecyl]-3α-ethyl-3,4-dihydro-2β-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyloxy)-2*H*-pyran-5-carboxylate* (**20**). Colourless oil, $[\alpha]_D^{28} = -105.3°$ ($c = 0.51$, $CHCl_3$). UV: 220.0 (4.08), 233.0 (4.11), 270.0 (2.82). IR: 3500, 1760, 1635, 1225, 1070, 1045. ^{1}H-NMR: 1.10–1.80 (*m*, 9 CH_2); 2.00–2.07 (4 OAc); 2.27 (*s*, arom. OAc); 2.58 (*t*, $J = 8.0$, CH_2(19)); 3.32 (*m*, H–C(7)); 3.74 (*s*, $COOCH_3$); 6.96–7.17 (*AA'BB'*, 4 arom. H); 7.50 (*s*, H–C(3)). ^{13}C-NMR: 10.7 (*q*, C(10)); 19.7 (*t*, C(8)); 26.0 (*t*, C(6)); 27.0 (*d*, C(5)); 29.2, 29.4, 29.7, 31.4, 35.3, 37.5, 38.2 (8*t*, C(12), C(13), C(14), C(15), C(16), C(17), C(18), C(19)); 41.3 (*d*, C(9)); 51.8 (*q*, $COOCH_3$); 67.5 (*d*, C(7)); 99.0 (*d*, C(1)); 110.7 (*s*, C(4)); 121.2 (*d*, C(22), C(24)); 129.3 (*d*, C(21), C(25)); 140.4 (*s*, C(20)); 148.7 (*s*, C(23)); 153.8 (*d*, C(3)); 169.4 (*s*, C(11)). Anal. calc. for $C_{41}H_{58}O_{16}\cdot H_2O$: C 59.70, H 7.33; found: C 59.92, H 7.27.

*Methyl 4α-[6(*R*)-10-(*p*-Acetoxyphenyl)-6-hydroxydecyl]-3α-ethyl-3,4-dihydro-2β-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyloxy)-2*H*-pyran-5-carboxylate* (**21**). White powder, $[\alpha]_D^{22} = -81.2°$ ($c = 0.70$, $CHCl_3$). UV: 227.0 (4.38). IR: 3500, 1760, 1710, 1630, 1370, 1220, 1070, 1040. ^{1}H-NMR: 0.94 (*t*, $J = 8.0$, CH_3(10)); 1.10–1.80 (*m*, 9 CH_2); 1.98–2.08 (4 OAc); 2.28 (*s*, arom. OAc); 2.58 (*t*, $J = 8.0$, CH_2(19)); 3.68 (*s*, $COOCH_3$); 3.44–3.84 (*m*, H–C(15)), 6.94–7.16 (*AA'BB'*, 4 arom. H); 7.33 (*s*, H–C(3)). ^{13}C-NMR: 11.4 (*q*, C(10)); 19.0 (*t*, C(8)); 25.3, 25.5 (2*t*, C(6), C(7)); 27.2 (*d*, C(5)); 29.0, 29.9, 30.0, 31.5, 35.3, 37.3, 37.5 (7*t*, C(12), C(13), C(14), C(16), C(17), C(18), C(19)); 40.5 (*d*, C(9)); 51.2 (*q*, $COOCH_3$); 71.6 (*d*, C(15)); 96.9, 97.8 (2*d*, C(1), anom. C); 112.0 (*s*, C(4)); 121.3 (*d*, C(22); C(24)); 129.3 (*d*, C(21), C(25)); 140.3 (*s*, C(20)); 148.8 (*s*, C(23)); 151.3 (*d*, C(3)); 167.8 (*s*, C(11)). Anal. calc. for $C_{41}H_{58}O_{16}\cdot H_2O$: C 59.70, H 7.33; found: C 59.48, H 7.57.

trans-*Tetrahydropyran* **22** (= *Methyl 4α-{[6β-[4-(*p*-Acetoxyphenyl)butyl]-3,4,5,6-tetrahydro-2*H*-pyran-2α-yl]methyl}-3α-ethyl-3,4-dihydro-2β-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyloxy)-2*H*-pyran-5-carboxylate*). White powder, $[\alpha]_D^{25} = -98.0°$ ($c = 0.97$, $CHCl_3$). UV: 220.0 (4.03), 228.5 (4.03). IR: 1760, 1710, 1630, 1370, 1220, 1070, 1040. ^{1}H-NMR: 0.95 (*t*, $J = 7.0$, CH_3(10)); 1.10–1.80 (*m*, 8 CH_2); 1.97–2.05 (4 OAc); 2.26 (*s*, arom. OAc); 2.61 (*t*, $J = 8.0$, CH_2(19)); 3.68 (*s*, $COOCH_3$); 3.72 (*m*, H–C(7), H–C(15)); 6.95–7.16 (*AA'BB'*, 4 arom. H); 7.30 (*s*, H–C(3)). ^{13}C-NMR: 11.6 (*q*, C(10)); 18.6 (*t*, C(13)); 19.0 (*t*, C(8)); 25.6 (*t*, C(6)); 27.8 (*d*, C(5)); 30.0, 30.3, 31.6, 33.0, 33.2, 35.4 (6*t*, C(12), C(14), C(16), C(17), C(18), C(19)); 40.5 (*d*, C(9)); 51.2 (*q*, $COOCH_3$); 69.0, 71.1 (2*d*, C(7), C(15)); 96.7, 97.4 (2*d*, C(1), anom. C); 112.7 (*s*, C(4)); 121.3 (*d*, C(22), C(24)); 129.3 (*d*,

C(21), C(25)); 140.3 (*s*, C(20)); 148.8 (*s*, C(23)); 151.1 (*d*, C(3)); 167.4 (*s*, C(11)). MS (EI): 804 (M^+), 331 ($^+$OGlcAc$_4$). Anal. calc. for $C_{41}H_{56}O_{16}$: C 61.18, H 7.01; found: C 60.96, H 7.10.

cis-*Tetrahydropyran* **23** (= cis-*Isomer of* **22**). White powder, $[\alpha]_D^{25} = -71.5°$ ($c = 0.94$, $CHCl_3$). UV: 220.0 (4.09), 229.0 (4.10). IR: 1760, 1710, 1630, 1220, 1075, 1045. ^{1}H-NMR: 1.10–1.80 (*m*, 9 CH_2); 1.93 (*t*, $J = 6.0$, CH_3(10)); 1.99–2.06 (4 OAc); 2.26 (*s*, arom. OAc); 2.58 (*t*, $J = 7.0$, CH_2(19)); 3.20 (*m*, H–C(7), H–C(15)); 3.65 (*s*, $COOCH_3$); 6.92–7.14 (*AA'BB'*, 4 arom. H); 7.31 (*s*, H–C(3)). ^{13}C-NMR: 11.1 (*q*, C(10)); 19.3 (*t*, C(8)); 23.8 (*t*, C(13)); 25.2 (*t*, C(6)); 27.5 (*d*, C(5)); 31.5, 32.2, 35.4, 36.5 (6*t*, C(12), C(14), C(16), C(17), C(18), C(19)); 40.8 (*d*, C(9)); 51.2 (*q*, $COOCH_3$); 75.6, 77.5 (2*d*, C(7), C(15)); 98.6 (*d*, C(1)); 113.1 (*s*, C(4)); 121.2 (*d*, C(22), C(24)); 129.3 (*d*, C(21), C(25)); 140.4 (*s*, C(20)); 148.7 (*s*, C(23)); 151.6 (*d*, C(3)); 167.7 (*s*, C(11)). Anal. calc. for $C_{41}H_{56}O_{16}$: C 61.18, H 7.01; found: C 60.98, H 6.95.

*(7*R*)-Lactone* **24** (= *3β-[8-(*p*-Acetoxyphenyl)octyl]-5α-ethyl-4,4aβ,5,6-tetrahydro-6β-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyloxy)-1*H,*3*H*-pyrano[3,4-*c*]pyran-1-one*). White powder, $[\alpha]_D^{27} = -75.7°$ ($c = 1.01$, $CHCl_3$). UV: 210.0 (3.98), 219.0 (3.99), 240.0 (3.95). IR: 1760, 1710, 1630, 1375, 1220, 1065, 1045. ^{1}H-NMR: 1.33 (br. *s*, 7 CH_2); 1.94–2.07 (4 OAc); 2.26 (*s*, arom. OAc); 2.59 (*t*, $J = 8.0$, CH_2(19)); 2.90–3.20 (*m*, H–C(5)); 4.30–4.60 (*m*, H–C(7)); 5.42 (*d*, $J = 1.0$, H–C(1)); 6.96–7.17 (*AA'BB'*, 4 arom. H); 7.45 (*d*, $J = 2.0$, H–C(3)). Anal. calc. for $C_{40}H_{54}O_{15}$: C 62.00, H 7.02; found: C 62.32, H 7.25.

*3α-[8-(*p*-Acetoxyphenyl)-4-oxooctyl]-5α-ethyl-4,4aβ,5,6-tetrahydro-6β-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyloxy)-1*H,*3*H*-pyrano[3,4-*c*]pyran-1-one* (**25**). White powder, $[\alpha]_D^{22} = -90.8°$ ($c = 1.03$, $CHCl_3$). UV: 210.0 (4.22), 219.0 (4.26), 227.0 (4.29), 238.0 (4.24). IR: 1760, 1710, 1625, 1220, 1060, 1040. ^{1}H-NMR: 1.95–2.08 (4 OAc); 2.27 (*s*, arom. OAc); 4.08–4.40 (*m*, H–C(7)); 5.40 (br. *s*, H–C(1)); 6.95–7.15 (*AA'BB'*, 4 arom. H); 7.48 (*d*, $J = 2.0$, H–C(3)). ^{13}C-NMR: 11.8 (*q*, C(10)); 17.5 (*t*, C(8)); 19.0, 23.3 (2*t*, C(12), C(13)); 28.2 (*d*, C(5)); 29.5, 30.9, 35.0, 35.2 (4*t*, C(6), C(17), C(18), C(19)); 37.6 (*d*, C(9)); 42.1, 42.4 (2*t*, C(14), C(16)); 79.2 (*d*, C(7)); 95.7, 96.1 (*d*, C(1), anom. C); 105.4 (*s*, C(4)); 121.4 (*d*, C(22), C(24)); 129.2 (*d*, C(21), C(25)); 139.7 (*s*, C(20)); 148.9 (*s*, C(23); 151.4 (*d*, C(3)); 165.5 (*s*, C(11)); 210.2 (*s*, C(15)). Anal. calc. for $C_{40}H_{52}O_{16}$: C 60.90, H 6.64; found: C 61.18, H 6.73.

cis-*Tetrahydropyran* **37** (= *7-Epi-***22**), $[\alpha]_D^{26} = -99.9°$ ($c = 0.97$, $CHCl_3$). UV: 220.0 (4.08), 227.5 (4.10), 270.0 (2.78). IR: 1760, 1710, 1630, 1220, 1075, 1040. ^{1}H-NMR: 0.94 (*t*, $J = 8.0$, CH_3(10)); 2.02–2.06 (4 OAc); 2.27 (*s*, arom. OAc); 2.60 (*t*, $J = 7.0$, CH_2(19)); 2.84 (*m*, H–C(5)); 3.20 (*m*, H–C(7), H–C(15)); 3.66 (*s*, $COOCH_3$); 6.94–7.06 (*AA'BB'*, 4 arom. H); 7.36 (*s*, H–C(3)). ^{13}C-NMR: 11.0 (*q*, C(10)); 19.3 (*t*, C(8)); 23.7 (*t*, C(13)); 25.2 (*t*, C(6)); 27.6 (*d*, C(5)); 31.4, 31.6, 31.7, 35.3, 36.4, 36.5 (6*t*, C(12), C(14), C(16), C(17), C(18), C(19)); 40.8 (*d*, C(9)); 51.1 (*q*, $COOCH_3$); 75.6, 77.7 (2*d*, C(7), C(15)); 97.2, 98.2 (2*d*, C(1), anom. C); 111.9 (*s*, C(4)); 121.3 (*d*, C(22), C(24)); 129.3 (*d*, C(21), C(25)); 140.3 (*s*, C(20)); 148.8 (*s*, C(23)); 151.9 (*d*, C(3)); 167.8 (*s*, C(11)). Anal. calc. for $C_{41}H_{56}O_{16}$: C 61.18, H 7.01; found: C 60.92, H 7.12.

8. *Methyl 4α-[(2*R*)-2-Acetoxy-10-(*p*-acetoxyphenyl)decyl]-3α-ethyl-3,4-dihydro-2β-(2,3,4,6-tetra-*O*-acetyl-*D*-glucopyranosyloxy)-2*H*-pyran-5-carboxylate* (**26**). Colourless oil, $[\alpha]_D^{27} = -83.9°$ ($c = 1.00$, $CHCl_3$). UV: 220.0 (4.10), 227.5 (4.10), 270.0 (2.80). IR: 1760, 1710, 1635, 1370, 1220, 1070, 1045. ^{1}H-NMR: 1.98 (*t*, $J = 7.0$, CH_3(10)); 1.99–2.08 (5 OAc); 2.27 (*s*, arom. OAc); 2.58 (*t*, $J = 8.0$, CH_2(19)); 3.67 (*s*, $COOCH_3$); 6.96–7.16 (*AA'BB'*, 4 arom. H); 7.34 (*s*, H–C(3)). Anal. calc. for $C_{43}H_{60}O_{17}$: C 60.84, H 7.12; found: C 60.98, H 7.35.

9. *Methyl 4α-[(6*R*)-6-Acetoxy-10-(*p*-acetoxyphenyl)decyl]-3α-ethyl-3,4-dihydro-2β-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyloxy)-2*H*-pyran-5-carboxylate* (**27**). Colourless oil, $[\alpha]_D^{27} = -81.3°$ ($c = 1.01$, $CHCl_3$). UV: 220.0 (4.06), 227.5 (4.07), 270.0 (2.76). IR: 1760, 1720, 1640, 1230, 1080, 1050. ^{1}H-NMR: 0.96 (*t*, $J = 7.0$, CH_3(10)); 2.00–2.08 (5 OAc); 2.28 (*s*, arom. OAc); 2.60 (*t*, $J = 8.0$, CH_2(19)); 3.68 (*s*, $COOCH_3$); 6.96–7.16 (*AA'BB'*, 4 arom. H); 7.34 (*s*, H–C(3)). Anal. calc. for $C_{43}H_{60}O_{17}$: C 60.84, H 7.12; found: C 61.12, H 7.18.

10. *(7*S*)-Lactone* **28** (= *7-Epi-***24**). MsCl (0.15 ml) was added to a solution of **20** (104 mg) in pyridine (1.5 ml) under ice cooling, and the whole was allowed to stand at r.t. for 5 h. After addition of H_2O (0.5 ml), the mixture was further stirred for 1 h at 50–60°, and then poured onto ice-cold H_2O (100 ml) and extracted with $CHCl_3$ (2 × 50 ml). The $CHCl_3$ layer was washed successively with 5% HCl, H_2O, 5% $NaHCO_3$, and H_2O, dried, and concentrated *in vacuo* to give a residue (99 mg), which was chromatographed on prep. TLC plates with benzene/Et_2O 5:1 (5 developments). A main band afforded **28** (51 mg) as a white powder, $[\alpha]_D^{26} = -114.3°$ ($c = 0.81$, $CHCl_3$). UV: 210.0 (3.99), 218.0 (4.01), 241.0 (4.00). IR: 1760, 1710, 1630, 1370, 1220, 1065, 1040. ^{1}H-NMR: 1.31 (br. *s*, 7 CH_2); 1.95–2.08 (4 OAc); 2.26 (*s*, arom. OAc); 2.59 (*t*, $J = 8.0$, CH_2(19)); 2.70–3.03 (*m*, H–C(5)); 4.20–4.80 (*m*, H–C(7)); 5.41 (*d*, $J = 1.5$, H–C(1)); 6.96–7.17 (*AA'BB'*, 4 arom. H); 7.50 (*d*, $J = 2.0$, H–C(3)). Anal. calc. for $C_{40}H_{54}O_{15}$: C 62.00, H 7.02; found: C 61.62, H 7.28.

11. *8-(*p*-Hydroxyphenyl)octan-1-ol* (**32**). A solution of 7-bromohept-1-yl tetrahydropyranyl ether (**31**) [14] (8.45 g) in THF (1.5 ml) was added dropwise to a stirred suspension of Mg (0.95 g) and I_2 (0.14 g) in THF (1 ml) in a N_2 stream at 4°. After stirring at 90° for 1 h, a solution of *p*-(benzyloxy)benzaldehyde (7.70 g) in THF

(30 ml) was added to the mixture at 4°, and the whole was allowed to stand overnight at r.t. The mixture was poured onto ice-cold H_2O (300 ml) and extracted with $CHCl_3$ (2 × 150 ml). The $CHCl_3$ layer was washed successively with H_2O, 5% HCl, and H_2O, dried, and concentrated *in vacuo*. The residue (15.1 g) was chromatographed on silica gel (360 g) with $CHCl_3$, collecting 50-ml fractions. *Fractions 7–11* gave a condensation product (5.40 g) as a colourless oil. This compound was hydrogenated over 30% Pd/C (1.2 g) in MeOH (100 ml) at r.t. until uptake of H_2 ceased. After removal of the catalyst, the filtrate was concentrated *in vacuo* to give a residue (3.35 g), which was dissolved in EtOH (40 ml) containing pyridinium *p*-toluenesulfonate (0.8 g). After stirring at 60° for 4 h, the mixture was slightly basified with K_2CO_3 and then concentrated *in vacuo*. The residue was taken up in AcOEt (2 × 150 ml), and the AcOEt layer was washed with H_2O, dried, and concentrated *in vacuo* to give a solid (3.28 g), which was recrystallized from $CHCl_3$/hexane to give **32** as colourless plates, m.p. 73.5°. UV: 224.5 (3.84), 278.5 (3.23). IR: 3350, 3150, 1590, 1510, 1205, 820. ^{1}H-NMR: 2.50 (br. *t*, J = 7.0, CH_2(8)); 2.72 (br. *s*, OH); 3.63 (br. *t*, J = 6.0, CH_2(1)); 6.75–7.02 (*AA'BB'*, 4 arom. H). Anal. calc. for $C_{14}H_{22}O_2$: C 75.63, H 9.97; found: C 75.43, H 9.80.

12. *8-(*p*-Benzyloxyphenyl)octyl Bromide* (**33**). Compound **32** (1.07 g) was dissolved in benzene (30 ml) containing Ph_3P (2.52 g) and CBr_4 (1.60 g), and the mixture was stirred for 1.5 h in a stream of N_2. Removal of the resultant Ph_3PO followed by evaporation of benzene afforded a residue (6.72 g), which was chromatographed on silica gel (70 g) with hexane and $CHCl_3$. The $CHCl_3$ eluate gave 8-(*p*-hydroxyphenyl)octyl bromide (0.91 g) as a colourless oil. This compound was treated with $C_6H_5CH_2Br$ (1.02 g) and K_2CO_3 (2.53 g) in acetone (25 ml) for 11 h. The mixture was filtered, and the filtrate was concentrated *in vacuo* to give a residue (2.00 g), which was chromatographed on silica gel (40 g) with hexane and benzene. The benzene eluate gave **33** (0.44 g) as colourless needles, m.p. 37°. UV: 210.0 (4.18), 225.0 (4.11), 276.5 (3.23), 284.0 (3.15). IR: 1600, 1510, 1240, 1020. ^{1}H-NMR: 2.53 (br. *t*, J = 7.0, CH_2(8)); 3.37 (*t*, J = 7.0, CH_2(1)); 5.01 (*s*, $PhCH_2O$), 6.87–7.08 (*AA'BB'*, 4 arom. H); 7.37 (br. *s*, 5 arom. H). Anal. calc. for $C_{21}H_{27}BrO$: C 67.20, H 7.25; found: C 67.56, H 7.32.

13. *(7*R*)-Lactone* **24** *and (7*S*)-Lactone* **28** *from Secologanin Tetraacete* (**16**). A solution of **33** (224 mg) in THF (5 ml) was added dropwise to a suspension of Mg (20 mg) and I_2 (10 mg) in THF (0.5 ml) at r.t., and the mixture was stirred for 30 min at 80° in a stream of N_2. After cooling to 0–5°, a solution of **16** (332 mg) in THF (2 ml) was added, and the solution was stirred for 1 h at the same temp. The mixture was poured onto ice-cold H_2O (50 ml), and extracted with $CHCl_3$ (2 × 50 ml). The $CHCl_3$ layer was washed with H_2O, dried, and concentrated *in vacuo* to give a residue (539 mg), which was subjected to prep. TLC ($CHCl_3$/Et_2O, 3:1). The band at R_f *ca.* 0.45 gave recovered **16** (141 mg). The band at R_f *ca.* 0.67 gave a product (257 mg), an aliquot (181 mg) of which was dissolved in MeOH (20 ml) and hydrogenated over 10% Pd/C at r.t. for 2 h. The catalyst was filtered off, and the filtrate was concentrated *in vacuo*. The residue (168 mg) was acetylated and the product (180 mg) chromatographed by prep. TLC with benzene/Et_2O 3:1 (10 developments). The more polar compound (15 mg) was identical with **24**, and the less polar (44 mg) with **28** (mixed m.p., ^{1}H-NMR, IR, *etc.*).

14. *Hydrangenoside C Pentaacetate* (**40**). White powder, $[\alpha]_D^{25} = -92.8°$ (c = 1.05, $CHCl_3$). UV: 220.0 (4.12). IR: 1760, 1710, 1630, 1370, 1220, 1075, 1040. ^{1}H-NMR: 1.88–2.07 (4 OAc); 2.26 (*s*, arom. OAc); 3.68 (*s*, $COOCH_3$); 4.06 (*m*, H–C(7), H–C(15)); 6.99–7.24 (*AA'BB'*, 4 arom. H); 7.34 (br. *s*, H–C(3)). ^{13}C-NMR: 27.5 (*d*, C(5)); 30.8 (*t*, C(17)); 34.4, 35.1 (2*t*, C(6), C(16)); 44.1 (*d*, C(9)); 46.7, 47.0 (2*t*, C(12), C(14)); 51.2 (*q*, $COOCH_3$); 70.2, 71.6 (2*d*, C(7), C(15)); 96.0, 96.3 (2*d*, C(1), anom. C); 111.6 (*s*, C(4)); 120.5 (*t*, C(10)); 121.5 (*d*, C(20), C(22)); 129.5 (*d*, C(19), C(23)); 133.2 (*d*, C(8)); 138.9 (*s*, C(18)); 149.0 (*s*, C(21)); 150.8 (*d*, C(3)); 167.0 (*s*, C(11)); 207.1 (*s*, C(13)). Anal. calc. for $C_{39}H_{48}O_{17}\cdot H_2O$: C 58.05, H 6.24; found: C 58.02, H 6.21.

15. *Hydrangenoside D Pentaacetate* (**41**). Colourless needles (from EtOH), m.p. 140–141°, $[\alpha]_D^{25} = -104.0°$ (c = 1.06, $CHCl_3$). UV: 219.5 (4.42). IR: 1760, 1715, 1630, 1510, 1370, 1220, 1070, 1040. ^{1}H-NMR: 1.34 (*m*, CH_2(6)); 1.90–2.02 (4 OAc); 2.26 (*s*, arom. OAc); 3.46 (*m*, H–C(7), H–C(15)); 7.02–7.28 (*AA'BB'*, 4 arom. H); 7.35 (*s*, H–C(3)). ^{13}C-NMR: 25.5 (*d*, C(5)); 30.4 (*t*, C(17)); 34.0, 37.1 (2*t*, C(6), C(16)); 42.3 (*d*, C(9)); 48.2 (*t*, C(12) or C(14)); 51.1 (*t*, C(14) or C(12); *q*, $COOCH_3$); 75.2, 77.7 (2*d*, C(7), C(15)); 95.6, 96.2 (2*d*, C(1), anom. C); 111.2 (*s*, C(4)); 120.6 (*t*, C(10)); 121.5 (*d*, C(20), C(22)); 129.6 (*d*, C(19), C(23)); 133.0 (*d*, C(8)); 138.9 (*s*, C(18)); 149.0 (*s*, C(21)); 150.5 (*d*, C(3)); 166.7 (*s*, C(11)); 206.7 (*s*, C(13)). MS (EI): 788 (M^+), 331 ($^+$OGlcAc$_4$), 165 (**15**). Anal. calc. for $C_{39}H_{48}O_{17}$: C 59.39, H 6.13; found: C 59.18, H 6.11.

16. *Isolation of Glucosides from* Hydrangea scandens. Air-dried leaves (2.76 kg) of *H. scandens* collected in Ichimonzi-mura (Tokushima Pref.) were powdered and extracted with hot MeOH (3 × 22 l) for 1 h. The combined extracts were concentrated *in vacuo*, and the residue (296 g) was digested in 50% MeOH (3 l). The insoluble part was filtered off through *Celite*, which was washed with 50% MeOH (2 l). The combined filtrate and washings, after concentration to 2 l, was extracted with BuOH (2 × 10 l). The residue (197 g) of the BuOH extract was chromatographed on silica gel (1.5 kg) with MeOH/$CHCl_3$ with increasing MeOH contents. The 12, 13, 18, and 19% MeOH/$CHCl_3$ eluates gave residues *R-1* (12.1 g), *R-2* (22.5 g), *R-3* (3.5 g), and *R-4* (13.6 g),

resp. *R-1* was rechromatographed on silica gel (600 g) with MeOH/AcOEt with increasing MeOH contents. The 8% MeOH/AcOEt fraction (6.45 g) was then subjected to medium-pressure column chromatography on silica gel (550 g, 1–2 kg/cm^2). Elution with 10% MeOH/$CHCl_3$ afforded a crystalline compound (5.35 g), which was identical with hydrangenoside D (**4**) isolated from *H.macrophylla* Ser. var. *macrophylla*. *R-2* was found to be identical with hydrangenoside C (**3**), also obtained from the above plant. *R-3* was chromatographed on silica gel (210 g) with MeOH/$CHCl_3$ with increasing MeOH contents. The 16% MeOH/$CHCl_3$ eluate furnished a glucoside fraction (1.43 g), which was then subjected to medium-pressure column chromatography on silica gel (140 g, 3–5 kg/cm^2). Elution with 10% MeOH/$CHCl_3$ yielded first hydrangenoside E (**5**) (0.84 g) and then hydrangenoside G (7) (0.49 g). *R-4* was also chromatographed on silica gel (550 g) with MeOH/$CHCl_3$ with increasing MeOH contents. The 20% MeOH/$CHCl_3$ eluate furnished hydrangenoside F (**6**) (7.00 g).

Hydrangenoside E (= *Methyl 3α-Ethenyl-2β-(β-*D*-glucopyranosyloxy)-3,4-dihydro-4α-{[3,4,5,6-tetrahydro-4α-hydroxy-6β-[2-(*p*-hydroxyphenyl)ethyl]-2*H*-pyran-2β-yl]methyl}-2*H*-pyran-5-carboxylate;* **5**). $[\alpha]_D^{25} = -108.7°$ ($c = 0.63$, MeOH). UV: 225.0 (4.12), 277.5 (3.20), 285.0 (3.11). IR: 3400, 1690, 1625, 1520, 1080. ^{1}H-NMR: 1.48 (*m*, CH_2(6), CH_2(12), CH_2(14), CH_2(16)); 2.62 (*t*, $J = 7.0$, CH_2(17)); 3.64 (*s*, $COOCH_3$); 4.06 (*m*, H–C(13)); 4.64 (*d*, $J = 7.0$, anom. H); 6.70–7.03 (*AA'BB'*, 4 arom. H); 7.38 (*s*, H–C(3)). ^{13}C-NMR: 28.5 (*d*, C(5)); 31.7 (*t*, C(17)); 35.8 (*t*, C(6)); 39.2, 39.7, 40.9 (3*t*, C(12), C(16), C(14)); 44.7 (*d*, C(9)); 51.7 (*q*, $COOCH_3$); 65.4 (*d*, C(13)); 69.9, 71.6 (2*d*, C(7), C(15)); 100.0 (*d*, C(1)); 112.1 (*d*, C(4)); 116.3 (*d*, C(20), C(22)); 120.0 (*t*, C(10)); 130.7 (*d*, C(19), C(23)); 134.5 (*s*, C(18)); 135.6 (*d*, C(8)); 152.9 (*d*, C(3)); 156.3 (*s*, C(21)); 169.4 (*s*, C(11)). MS (FAB): 603 ($(M + Na)^+$), 581 ($(M + 1)^+$), 441 ($[(M + Na)-162]^+$), 419 ($[(M + 1)-162]^+$), 401 ($[(M + 1)-180]^+$). Anal. calc. for $C_{29}H_{40}O_{12} \cdot H_2O$: C 58.18, H 7.07; found: C 57.98, H 7.18.

Hydrangenoside F (= *7-Epihydrangenoside E;* **6**). $[\alpha]_D^{25} = -87.0°$ ($c = 1.00$, MeOH). UV: 226.5 (4.18), 277.5 (3.24). IR: 3400, 1690, 1630, 1515, 1290, 1080. ^{1}H-NMR: 1.75 (*m*, CH_2(6), CH_2(12), CH_2(14), CH_2(16)); 2.57 (*m*, CH_2(17)); 3.68 (*s*, $COOCH_3$); 6.70–7.07 (*AA'BB'*, 4 arom. H); 7.42 (*s*, H–C(3)). MS (FAB): 603 ($(M + Na)^+$), 581 ($(M + 1)^+$), 441 ($[(M + Na)-162]^+$), 419 ($[(M + 1)-162]^+$). Anal. calc. for $C_{29}H_{40}O_{12} \cdot 2H_2O$: C 56.48, H 7.19; found: C 56.76, H 7.01.

Hydrangenoside G (= *Methyl 3α-Ethenyl-2β-(β-*D*-glucopyranosyloxy)-4α-[(6*S*)-6-hydroxy-8-(*p*-hydroxyphenyl)-4-oxo-2-octenyl]-2*H*-pyran-5-carboxylate;* 7). $[\alpha]_D^{26} = -104.1°$ ($c = 1.00$, MeOH). UV: 227.0 (4.34), 278.5 (3.33). IR: 3400, 2925, 1700, 1630, 1440, 1070. ^{1}H-NMR: 1.68 (*m*, CH_2(16)); 2.62 (*m*, H–C(5), CH_2(6), H–C(9), CH_2(14), CH_2(17)); 3.60 (*s*, $COOCH_3$); 4.62 (*d*, $J = 8.0$, anom. H); 5.96 (*d*, $J = 16.0$, H–C(12)); 6.68–6.96 (*AA'BB'*, 4 arom. H); 7.43 (*s*, H–C(3)). ^{13}C-NMR: 31.8, 33.8, 40.3 (3*t*, C(6), C(16), C(17)); 33.3 (*d*, C(5)); 45.1 (*d*, C(9)); 51.9 (*q*, $COOCH_3$); 97.5, 100.0 (2*d*, C(1), anom. C); 110.2 (*s*, C(4)); 116.2 (*d*, C(20), C(22)); 120.1 (*t*, C(10)); 130.3 (*d*, C(19), C(23)); 132.9 (*d*, C(12)); 134.0 (*s*, C(18)); 135.0 (*d*, C(8)); 148.4 (*d*, C(7)); 153.9 (*d*, C(3)); 156.1 (*s*, C(21)); 168.9 (*s*, C(11)); 201.7 (*s*, C(13)). MS (FAB): 601 ($(M + Na)^+$), 579 ($(M + 1)^+$), 417 ($[(M + 1)-162]^+$), 399 ($[(M + 1)-180]^+$). Anal. calc. for $C_{29}H_{38}O_{12} \cdot H_2O$: C 58.38, H 6.76; found: C 58.11, H 6.92.

17. *Hydrangenoside E Hexaacetate* (**42**). White powder, $[\alpha]_D^{25} = -95.5°$ ($c = 0.99$, $CHCl_3$). UV: 220.0 (4.11), 270.0 (2.74). IR: 1765, 1715, 1630, 1225, 1065, 1040. ^{1}H-NMR: 1.90–2.06 (*s*, 5 OAc); 2.28 (*s*, arom. OAc); 3.08 (*m*, H–C(9)); 3.52 (*m*, H–C(7), H–C(15)); 3.67 (*s*, $COOCH_3$); 7.00–7.27 (*AA'BB'*, 4 arom. H); 7.32 (*d*, $J = 1.5$, H–C(1)). ^{13}C-NMR: 26.3 (*d*, C(5)); 30.7 (*t*, C(17)); 34.2, 35.9, 36.1, 37.4 (4*t*, C(6), C(12), C(14), C(16)); 42.8 (*d*, C(9)); 51.2 (*q*, $COOCH_3$); 68.3, 70.6 (2*d*, C(7), C(15)); 68.9 (*d*, C(13)); 95.8, 96.5 (2*d*, C(1), anom. C); 111.8 (*s*, C(4)); 119.8 (*t*, C(10)); 121.4 (*d*, C(20), C(22)); 129.7 (*d*, C(19), C(23)); 133.7 (*d*, C(8)); 140.0 (*s*, C(18)); 148.9 (*s*, C(21)); 150.5 (*d*, C(3)); 167.2 (*s*, C(11)). Anal. calc. for $C_{41}H_{52}O_{18} \cdot \frac{1}{2}H_2O$: C 58.50, H 6.35; found: C 58.31, H 6.38.

18. *$NaBH_4$ Reduction of Hydrangenoside D Pentaacetate* (**41**). $NaBH_4$ (188 mg) was added to a solution of **41** (2300 mg) in MeOH (70 ml) and the whole was stirred for 5 min at r.t. Excess reagent was decomposed by adding AcOH, and the solvent was evaporated *in vacuo*. The residue was taken up in $CHCl_3$, and the $CHCl_3$ layer was washed successively with H_2O, 5% HCl, H_2O, 5% $NaHCO_3$, and H_2O, dried, and concentrated. The residue was chromatographed on silica gel (300 g). Elution with 80% Et_2O/$CHCl_3$ afforded *hydrangenoside E pentaacetate* (**43**, 245 mg) and *13-epi-hydrangenoside E pentaacetate* (**44**, 1839 mg). **43**: White powder, $[\alpha]_D^{28} = -99.7°$ ($c = 1.00$, $CHCl_3$). UV: 219.5 (4.08), 271.0 (2.72). IR: 3480, 1760, 1715, 1630, 1225, 1065, 1040. ^{1}H-NMR: 1.92–2.06 (*s*, 4 OAc); 2.27 (*s*, arom. OAc); 3.48–3.88 (*m*, H–C(7), H–C(13), H–C(15)); 3.67 (*s*, $COOCH_3$); 6.98–7.26 (*AA'BB'*, 4 arom. H); 7.36 (*s*, H–C(3)). ^{13}C-NMR: 26.7 (*d*, C(5)); 30.8 (*t*, C(17)); 34.5, 37.5 (2*t*, C(6), C(16)); 38.8, 39.0 (2*t*, C(12), C(14)); 42.8 (*d*, C(9)); 51.2 (*q*, $COOCH_3$); 64.7 (*d*, C(13)); 68.3, 70.4 (2*d*, C(7), C(15)); 96.0, 96.5 (2*d*, C(1), anom. C); 111.8 (*s*, C(4)); 120.0 (*t*, C(10)); 121.3 (*d*, C(20), C(22); 129.6 (*d*, C(19), C(23)); 133.5 (*d*, C(8)); 140.1 (*s*, C(18)); 148.8 (*s*, C(21)); 150.7 (*d*, C(3)); 167.4 (*s*, C(11)). Anal. calc. for $C_{39}H_{50}O_{17} \cdot \frac{1}{2}H_2O$: C 58.57, H 6.43; found: C 58.33, H 6.46. Acetylation of **43** yielded **42**, identical with **42**

obtained from **5**. **44**: Colourless needles (Et_2O/petroleum ether), m.p. 130–132°, $[\alpha]_D^{29} = -102.6°$ ($c = 1.05$, $CHCl_3$). UV: 225.0 (4.14), 277.5 (3.02). IR: 3480, 1760, 1715, 1630, 1220, 1070, 1040. ^{1}H-NMR: 1.90–2.03 (*s*, 4 OAc); 2.26 (*s*, arom. OAc); 2.37 (br. *s*, OH); 3.13 (*m*, H–C(7), H–C(15)); 3.60–3.90 (*m*, H–C(13)); 3.69 (*s*, $COOCH_3$); 6.98–7.22 (*AA'BB'*, 4 arom. H); 7.31 (*s*, H–C(3)). ^{13}C-NMR: 26.3 (*d*, C(5)); 30.7 (*t*, C(17)); 34.1, 37.1 (2*t*, H–C(6), H–C(16)); 41.4, 41.6 (2*t*, H–C(12), H–C(14)); 42.6 (*d*, H–C(9)); 51.2 (*q*, $COOCH_3$); 68.0 (*d*, H–C(13)); 72.1, 73.8 (2*d*, C(7), C(15)); 95.8, 96.5 (2*d*, C(1), anom. C); 111.7 (*s*, C(4)); 120.0 (*t*, C(10)); 121.3 (*d*, C(20), C(22)); 129.6 (*d*, C(19), C(23)); 133.5 (*d*, C(8)); 139.8 (*s*, C(18)); 148.8 (*s*, C(21)); 150.5 (*d*, C(3)); 167.2 (*s*, C(11)). Anal. calc. for $C_{39}H_{50}O_{17} \cdot H_2O$: C 57.91, H 6.48; found: C 57.97, H 6.30. Acetylation of **44** yielded 13-epihydrangenoside E hexaacetate (**45**), colourless needles (EtOH), m.p. 86–89°, $[\alpha]_D^{31} = -96.2°$ ($c = 0.94$, $CHCl_3$). UV: 225.0 (4.14), 277.5 (2.97). IR: 1765, 1715, 1630, 1220, 1075, 1045. ^{1}H-NMR: 1.90–2.02 (*s*, 5 OAc); 2.26 (*s*, arom. OAc); 3.17 (*m*, H–C(7), H–C(15)); 3.68 (*s*, $COOCH_3$); 6.98–7.23 (*AA'BB'*, 4 arom. H); 7.31 (*d*, $J = 1.5$, H–C(3)). Anal. calc. for $C_{41}H_{52}O_{18} \cdot \frac{1}{2}H_2O$: 58.50, H 6.35; found: C 58.44, H 6.21.

19. *Catalytic Reduction of Hydrangenoside F* (**6**). Glucoside **6** (400 mg) was hydrogenated in MeOH (50 ml) over 10% Pd/C (0.2 g) at r.t. for 1 h. After filtration and evaporation, the product (431 mg) was eluted from a silica-gel column (70 g) with MeOH/$CHCl_3$ with increasing MeOH contents. The 15% MeOH/$CHCl_3$ eluate yielded *dihydrohydrangenoside F* (= *methyl 3α-ethyl-2β-(β-*D*-glucopyranosyloxy)-3,4-dihydro-4α-{[3,4,5,6-tetrahydro-4α-hydroxy-6β-[2-(*p*-hydroxyphenyl)ethyl]-2*H*-pyran-2α-yl]methyl}-2*H*-pyran-5-carboxylate*; **50**) (348 mg) as a white powder, $[\alpha]_D^{31} = -137.3°$ ($c = 0.99$, MeOH). UV: 228.0 (4.22), 278.0 (3.28), 285.0 (3.28). IR: 3400, 2950, 1700, 1630, 1515, 1070. ^{1}H-NMR: 1.00 (*t*, $J = 7.0$, CH_3(10)); 2.63 (*m*, CH_2(17)); 3.00 (*m*, H–C(5)); 3.67 (*s*, $COOCH_3$); 3.87 (*m*, H–C(7), H–C(15)); 5.43 (*d*, $J = 8.0$, H–C(1)); 6.70–7.07 (*AA'BB'*, 4 arom. H); 7.45 (*s*, H–C(3)). Anal. calc. for $C_{29}H_{42}O_{12} \cdot \frac{3}{2}H_2{=}O$: C 57.14, H 7.44; found: C 57.28, H 7.36.

20. *Dihydrohydrangenoside F Hexaacetate* (**48**). White powder, $[\alpha]_D^{27} = -111.5°$ ($c = 1.00$, $CHCl_3$). UV: 219.0 (4.07), 230.0 (4.10), 270.0 (2.69). IR: 1760, 1710, 1620, 1220, 1070, 1040. ^{1}H-NMR: 0.98 (*t*, $J = 8.0$, CH_3(10)); 1.98–2.05 (5 OAc); 2.25 (*s*, arom. OAc); 3.72 (*s*, $COOCH_3$); 3.97 (*m*, H–C(7), H–C(15)); 7.05–7.32 (*AA'BB'*, 4 arom. H); 7.41 (*s*, H–C(3)). Anal. calc. for $C_{41}H_{54}O_{18}$: C 58.99, H 6.52; found: C 59.15, H 6.67.

21. *Conversion of Hydrangenoside C Pentaacetate* (**40**) *into* **48** *and 13-Epidihydrohydrangenoside F Hexaacetate* (**49**). The $NaBH_4$-reduction product (3.60 g) of **40** was hydrogenated over 10% Pd/C (1.75 g) in MeOH (30 ml) for 1 h at r.t. After removal of the catalyst, the filtrate was concentrated *in vacuo*. The residue (3.90 g) was chromatographed on silica gel (350 g) with AcOEt/$CHCl_3$ with increasing AcOEt contents. The 90% AcOEt/$CHCl_3$ eluate gave first **46** (2.17 g) and then **47** (0.87 g), both as a white powder.

Dihydrohydrangenoside F Pentaacetate (**46**). $[\alpha]_D^{27} = -105.0°$ ($c = 1.00$, $CHCl_3$). UV: 219.0 (4.09), 229.5 (4.12), 270.5 (2.82). IR: 3475, 1765, 1715, 1635, 1225, 1070, 1040. ^{1}H-NMR: 1.00 (*t*, $J = 6.0$, CH_3(10)); 2.00–2.08 (4 OAc); 2.30 (*s*, arom. OAc); 3.68 (*s*, $COOCH_3$); 4.04 (*m*, H–C(7), H–C(13), H–C(15)); 7.04–7.30 (*AA'BB'*, 4 arom. H); 7.39 (*s*, H–C(3)). Anal. calc. for $C_{39}H_{52}O_{17}$: C 59.08, H 6.61; found: C 58.82, H 6.80.

Acetylation of **46** gave **48** (2.30 g), which was identical with **48** derived from **6** *(vide supra)*.

13-Epidihydrohydrangenoside F Pentaacetat (**47**); $[\alpha]_D^{25} = -106.4°$ ($c = 1.00$; $CHCl_3$). UV: 220.0 (4.09); 224.0 (4.09); 271.0 (2.82). IR: 3450, 1760, 1710, 1630, 1220, 1065, 1040. ^{1}H-NMR: 0.98 (*t*, $J = 6.0$, CH_3(10)); 2.00–2.10 (4 OAc); 2.30 (*s*, arom. OAc); 3.72 (*s*, $COOCH_3$); 4.21 (*m*, H–C(7), H–C(13), H–C(15)); 6.97–7.18 (*AA'BB'*, 4 arom. H); 7.30 (*s*, H–C(3)). Anal. calc. for $C_{39}H_{52}O_{17} \cdot \frac{1}{2}H_2O$: C 58.42, H 6.66; found: C 58.50, H 6.81.

Acetylation of **47** gave *13-epidihydrohydrangenoside F hexaacetate* (**49**; 0.86 g) as a white powder, $[\alpha]_D^{29} = -101.9°$ ($c = 1.12$; $CHCl_3$). UV: 220.0 (4.10); 228.0 (4.11); 270.0 (2.81). IR: 1760, 1630, 1220, 1070, 1040. ^{1}H-NMR: 0.97 (*t*, $J = 7.0$, CH_3(10)); 1.99–2.07 (4 OAc); 2.27 (*s*, arom. OAc); 2.69 (*t*, $J = 8.0$, CH_2(17)); 3.69 (*s*, $COOCH_3$); 3.77 (*m*, H–C(7) or H–C(15)); 4.10 (*m*, H–C(15) or H–C(7)); 6.95–7.18 (*AA'BB'*, 4 arom. H); 7.33 (*s*, H–C(3)).

22. *Dihydrohydrangenoside C Pentaacetate* (**51**). Compound **40** (1.07 g) was hydrogenated over 10% Pd/C (0.75 g) in AcOEt (40 ml) at r.t. for 1 h. The usual workup gave **51** (1.16 g) as a white powder, $[\alpha]_D^{25} = -98.1°$ ($c = 0.97$, $CHCl_3$). UV: 222.5 (4.16), 270.0 (2.85). IR: 1755, 1705, 1625, 1215, 1060, 1035. ^{1}H-NMR: 0.97 (*t*, $J = 7.0$, CH_3(10)); 1.97–2.07 (4 OAc); 2.27 (*s*, arom. OAc); 3.68 (*s*, $COOCH_3$); 4.00–4.43 (*m*, H–C(7), H–C(15)); 6.97–7.22 (*AA'BB'*, 4 arom. H); 7.33 (*s*, H–C(3)). Anal. calc. for $C_{39}H_{50}O_{17}$: C 59.23, H 6.37; found: C 59.05, H 6.51.

23. *Bromination of* **51**. A solution of Br_2 (0.65 g) in dry CH_2Cl_2 (5 ml) was added within 20 min to a stirred solution of **51** (3.00 g) in dry THF (30 ml) at 0–5°, and stirring was continued for further 10 min. The mixture was diluted with 5% $NaHCO_3$ (250 ml), and extracted with CH_2Cl_2 (2 × 250 ml). The CH_2Cl_2 layer was washed with H_2O, dried, and concentrated *in vacuo*. The residue (3.9 g) was chromatographed on silica gel (300 g) with AcOEt/benzene with increasing AcOEt contents. The 35% AcOEt/benzene eluate yielded a mixture **52** of

monobromides (2.2 g) as a white powder. IR: 1760, 1710, 1635, 1220, 1070, 1045. ^{1}H-NMR: 1.03 (*t*, *J* = 7.0, CH_3(10)); 1.98–2.09 (4 OAc); 2.29 (*s*, arom. OAc); 2.86 (*m*, CH_2(12), CH_2(14)); 3.70 (*s*, $OCOCH_3$); 4.13 (*m*, H–C(7), H–C(15)); 7.02–7.28 (*AA'BB'*, 4 arom. H); 7.37 (*s*, H–C(3)). Anal. calc. for $C_{39}H_{47}BrO_{17}$: C 53.99, H 5.46; found: C 53.70, H 5.71.

24. *Methyl 4α-{[2β-[2-(*p*-Acetoxyphenyl)ethyl]-3,4-dihydro-4-oxo-2*H*-pyran-6-yl]methyl}-3α-ethyl-3,4-dihydro-2β-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyloxy)-2*H*-pyran-5-carboxylate* (**53**) *and Methyl 4α-{[6-[2-(*p*-Acetoxyphenyl)ethyl]-3,4-dihydro-4-oxo-2*H*-pyran-2α-yl]methyl}-3α-ethyl-3,4-dihydro-2β-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyr anosyloxy)-2*H*-pyran-5-carboxylate* (**54**). Magnesium oxide (150 mg) was added to a stirred solution of **52** (1500 mg) in dry DMF (15 ml) under Ar. After stirring for a further 20 min at 125–130°, the mixture was cooled, diluted with 1N HCl, and extracted with $CHCl_3$. The $CHCl_3$ layer was washed with H_2O, dried, and concentrated *in vacuo*. The residue (1500 mg) was subjected to medium-pressure column chromatography on silica gel (80 g; 2–3 kg/cm^2). Elution with 30% AcOEt/$CHCl_3$ furnished first **53** (270 mg) and then **54** (862 mg). **53**: White powder, $[\alpha]_D^{25} = -159.4°$ (*c* = 0.64, $CHCl_3$). UV: 217.5 (4.11), 227.0 (4.13), 265.0 (4.18). IR: 1760, 1710, 1670, 1635, 1605, 1220, 1065, 1040. ^{1}H-NMR: 0.97 (*t*, *J* = 7.0, CH_3(10)); 1.97–2.06 (4 OAc); 2.28 (*s*, arom. OAc); 2.83 (*t*, *J* = 6.0, CH_2(17)); 3.20 (*m*, H–C(5)); 3.66 (*s*, $COOCH_3$); 4.33 (*m*, H–C(15)); 5.27 (*s*, H–C(12)); 7.00–7.22 (*AA'BB'*, 4 arom. H). ^{13}C-NMR: 11.2 (*q*, C(10)); 18.6 (*t*, C(8)); 28.7 (*d*, C(5)); 30.4 (*t*, C(17)); 34.4, 36.1 (2*t*, C(6), C(16)); 39.8 (*t*, C(14)); 41.0 (*d*, C(9)); 51.3 (*q*, $COOCH_3$); 78.1 (*d*, C(15)); 96.5, 96.7 (2*d*, C(1), anom. C); 105.7 (*d*, C(12)); 110.1 (*s*, C(4)); 121.7 (*d*, C(20), C(22)); 129.5 (*d*, C(19), C(23)); 138.5 (*s*, C(18)); 149.2 (*s*, C(21)); 151.8 (*d*, C(3)); 167.0 (*s*, C(11)); 175.2 (*s*, C(7)); 192.7 (*s*, C(13)). Anal. calc. for $C_{39}H_{46}O_{17}$: C 59.54, H 6.13; found: C 59.58, H 5.89.

54: White powder, $[\alpha]_D^{25} = -145.4°$ (*c* = 0.83, $CHCl_3$). UV: 233.0 (4.09), 263.0 (4.10). IR: 1760, 1710, 1670, 1632, 1610, 1220, 1070, 1040. ^{1}H-NMR: 1.00 (*t*, *J* = 7.0, CH_3(10)); 2.01–2.07 (4 OAc); 2.28 (*s*, arom. OAc); 3.68 (*s*, $COOCH_3$); 4.28 (*m*, H–C(7)); 5.27 (*s*, H–C(14)); 6.98–7.20 (*AA'BB'*, 4 arom. H); 7.40 (*s*, H–C(3)). ^{13}C-NMR: 11.1 (*q*, C(10)); 19.3 (*t*, C(8)); 27.0 (*d*, C(5)); 31.9 (*t*, C(17)); 35.0, 36.4 (2*t*, C(6), C(16)); 40.9 (*d*, C(9)); 41.7 (*t*, C(12)); 51.4 (*q*, $COOCH_3$); 77.7 (*d*, C(7)); 96.9, 97.6 (2*d*, C(1), anom. C); 104.6 (*d*, C(14)); 111.6 (*s*, C(4)); 121.6 (*d*, C(20), C(22)); 129.3 (*d*, C(19), C(23)); 138.0 (*s*, C(18)); 149.2 (*s*, C(21)); 152.4 (*d*, C(3)); 167.4 (*s*, C(11)); 176.3 (*s*, C(15)); 192.8 (*d*, C(13)). Anal. calc. for $C_{39}H_{46}O_{17}$: C 59.54, H 6.13; found: C 59.25, H 6.11.

25. *Methyl 4α-{[6-[2-(*p*-Acetoxyphenyl)ethyl]-3,4-dihydro-4α-hydroxy-2*H*-pyran-2α-yl]methyl}-3α-ethyl-3,4-dihydro-2β-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyloxy)-2*H*-pyran-5-carboxylate* (**55**). $NaBH_4$ (66 mg) was added to a solution of **54** (679 mg) in MeOH (8 ml) at 0–5°. After stirring for 1 h at 0–5°, the mixture was worked up in the usual way, and the product (693 mg) was subjected to medium-pressure column chromatography on silica gel (60 g; 1–2 kg/cm^2). Elution with 40% Et_2O/$CHCl_3$ afforded **55** (210 mg) as a white powder, $[\alpha]_D^{24} = -112.7°$ (*c* = 0.70, $CHCl_3$). UV: 217.5 (4.14), 265.0 (3.30). IR: 3460, 1758, 1705, 1630, 1220, 1062, 1038. ^{1}H-NMR: 0.99 (*t*, *J* = 7.0, CH_3(10)); 1.99–2.07 (4 OAc); 2.26 (*s*, arom. OAc); 2.80 (*m*, H–C(7)); 4.48 (*m*, H–C(13)); 6.96–7.17 (*AA'BB'*, 4 arom. H); 7.36 (*s*, H–C(3)). ^{13}C-NMR: 11.2 (*q*, C(10)); 19.1 (*t*, C(8)); 27.5 (*d*, C(5)); 32.6 (*t*, C(17)); 35.1, 35.8 (2*t*, C(6), C(16)); 38.4 (*t*, C(12)); 40.7 (*d*, C(9)); 51.3 (*q*, $COOCH_3$); 63.6 (*d*, C(13)); 73.2 (*d*, C(7)); 96.8, 97.6 (2*d*, C(1), anom. C); 101.1 (*d*, C(14)); 112.3 (*s*, C(4)); 121.4 (*d*, C(20), C(22)); 129.5 (*d*, C(19), C(23)); 139.3 (*s*, C(18)); 148.9 (*s*, C(21)); 151.9 (*d*, C(3)); 155.2 (*s*, C(15)); 167.5 (*s*, C(11)). Anal. calc. for $C_{39}H_{50}O_{17}$: C 59.24, H 6.37; found: C 59.54, H 6.41.

26. *Catalytic Reduction of* **55**. Compound **55** (184 mg) was hydrogenated over Pt (prepared from PtO_2 (300 mg)) in EtOH (3 ml) at r.t. for 1 h. After filtration and evaporation, the product (207 mg) was subjected to prep. TLC ($CHCl_3$/Et_2O 2:1, 5 developments). Of 2 major bands, the upper one gave a white powder (9 mg), whose acetylation yielded **48** identical with **48** obtained from **50**. The less polar band afforded *15-epi-dihydrohydrangenoside F pentaacetate* (**56**; 133 mg). $[\alpha]_D^{24} = -109.1°$ (*c* = 0.49, $CHCl_3$). UV: 215.0 (4.04), 226.0 (4.11), 268.0 (2.94). IR: 3450, 1760, 1710, 1630, 1220, 1070, 1040. ^{1}H-NMR: 0.98 (*t*, *J* = 7.0, CH_3(10)); 1.98–2.06 (4 OAc); 2.26 (*s*, arom. OAc); 2.72 (*t*, *J* = 7.0, CH_2(17)); 3.28 (*m*, H–C(7), H–C(15)); 3.66 (*s*, $COOCH_3$); 3.74 (*m*, H–C(13)); 6.94–7.18 (*AA'BB'*, 4 arom. H); 7.36 (*s*, HC(3)). ^{13}C-NMR: 11.1 (*q*, C(10)); 19.0 (*t*, C(8)); 27.3 (*d*, C(5)); 30.9 (*t*, C(17)); 35.4, 37.4 (2*t*, C(6), C(16)); 40.9, 41.0 (2*t*, C(12), C(14)); 41.4 (*d*, C(9)); 51.2 (*q*, $COOCH_3$); 68.0 (*d*, C(13)); 73.2, 74.4 (2*d*, C(7), C(15)); 97.0, 97.7 (2*d*, C(1), anom. C); 111.6 (*s*, C(4)); 121.4 (*d*, C(20), C(22)); 129.4 (*d*, C(19), C(23)); 139.7 (*s*, C(18)); 148.9 (*s*, C(21)); 151.8 (*d*, C(3)); 167.7 (*s*, C(11)). Anal. calc. for $C_{39}H_{52}O_{17}$: C 59.08, H 6.61; found: C 58.92, H 6.63.

27. *13-Epidihydrohydrangenoside E Pentaacetate* (**57**). Compound **44** (51 mg) was hydrogenated over 10% Pd/C (100 mg) in MeOH (20 ml) at r.t. for 30 min. The usual workup gave **57** (45 mg) as a white powder, $[\alpha]_D^{29} = -102.9°$ (*c* = 1.00, $CHCl_3$). UV: 226.0 (4.16), 279.0 (3.11). IR: 3550, 3500, 1762, 1710, 1220, 1070, 1045. ^{1}H-NMR: 0.93 (*t*, *J* = 7.0, CH_3(10)); 1.98–2.03 (4 OAc); 2.26 (*s*, arom. OAc); 2.45 (br. *s*, OH–C(13)); 2.69 (*t*, *J* = 8.0, CH_2(17)); 3.22 (*m*, H–C(7), H–C(15)); 3.67 (*s*, $COOCH_3$); 6.95–7.18 (*AA'BB'*, 4 arom. H); 7.37 (*s*,

H–C(3)). ^{13}C-NMR: 11.1 (*q*, C(10)); 19.3 (*t*, C(8)); 27.5 (*d*, C(5)); 31.2 (C(17)); 36.2, 38.0 (2*t*, C(6), C(16)); 40.9, 41.1 (2*t*, C(12), C(14)); 41.8 (*d*, C(9)); 51.2 (*q*, $COOCH_3$); 68.0 (*d*, C(13)); 73.4, 74.4 (2*d*, C(7), C(15)); 96.9, 98.0 (2*d*, C(1), anom. C); 112.8 (*s*, C(4)); 121.4 (*d*, C(20), C(22)); 129.4 (*d*, C(19), C(23)); 140.1 (*s*, C(18)); 149.8 (*s*, C(21)); 151.8 (*d*, C(3)); 167.7 (*s*, C(11)). Anal. calc. for $C_{39}H_{52}O_{17} \cdot \frac{1}{2}H_2O$: C 58.42, H 6.66; found: C 58.69, H 6.79.

28. *Hydrangenoside G Hexaacetate* (**58**). White powder, $[\alpha]_D^{24} = -95.1°$ (*c* = 1.00, $CHCl_3$). UV: 227.5 (4.29). IR: 1760, 1710, 1670, 1630, 1220, 1065, 1040. ^{1}H-NMR: 1.89–2.06 (5 OAc); 2.24 (*s*, arom. OAc); 3.64 (*s*, $COOCH_3$); 5.96 (*d*, *J* = 16.0, H–C(12)); 6.72 (*m*, H–C(7)); 6.94–7.14 (*AA'BB'*, 4 arom. H); 7.34 (*s*, H–C(3)). ^{13}C-NMR: 29.7 (*d*, C(5)); 31.1, 31.5 (2*t*, C(16), C(17)); 35.8 (*t*, C(6)); 43.1 (*d*, C(9)); 44.1 (*t*, C(14)); 51.3 (*q*, $COOCH_3$); 70.3 (*d*, C(15)); 96.0, 96.3 (2*d*, C(1), anom. C); 110.0 (*s*, C(4)); 120.8 (*t*, C(10)); 121.5 (*d*, C(20), C(22)); 129.3 (*d*, C(19), C(23)); 132.1 (*d*, C(12)); 132.3 (*d*, C(8)); 138.9 (*s*, C(18)); 145.7 (*d*, C(7)); 149.0 (*s*, C(21)); 151.2 (*d*, C(3)); 166.8 (*s*, C(11)); 196.8 (*d*, C(13)). Anal. calc. for $C_{41}H_{50}O_{18} \cdot H_2O$: C 58.01, H 6.17; found: C 58.24, H 6.10.

29. *Methyl 4α-[(6*R*)-6-Acetoxy-8-(*p*-acetoxyphenyl)octyl]-3α-ethyl-3,4-dihydro-2β-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyloxy)-2*H*-pyran-5-carboxylate* (**60**). $NaBH_4$ (15 mg) was added to a stirred solution of **58** (102 mg) in MeOH (7 ml) at −5 to 0°. After stirring for a further 30 min at −5 to 0°, the mixture was worked up in the usual way. The product (106 mg) was purified by prep. TLC ($CHCl_3$/Et_2O 2:1) to afford a mixture **59** (= *methyl 4α-[(6*R*)-6-acetoxy-8-(p-acetoxyphenyl)-4-hydroxy-2-octenyl]-3α-ethyl-3,4-dihydro-2β-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyloxy)-2H-pyran-5-carboxylate*) of 13-epimeric alcohols (79 mg) as a white powder. ^{1}H-NMR: 1.97–2.27 (10 OAc); 3.67, 3.68 (2*s*, $COOCH_3$); 4.00, 4.10 (2*m*, H–C(13)); 7.30, 7.31 (2*s*, H–C(3)). ^{13}C-NMR: 30.4, 30.9 (2*d*, C(5)); 31.0, 31.1, 31.4, 36.1, 36.5, 39.3, 41.8, 42.6 (8*t*, C(6), C(14), C(16), C(17)); 43.0, 43.2 (2*d*, C(9)); 51.2 (*q*, $COOCH_3$); 68.3, 70.1, 71.3, 71.7 (4*d*, C(13), C(15)); 96.0, 96.2, 96.6, 96.7 (4*d*, C(1), anom. C); 110.7 111.0 (2*s*, C(4)); 119.9, 120.2 (2*t*, C(10)); 121.5 (*d*, C(20), C(22)); 128.4, 130.3 (2*d*, C(7)); 129.3, 129.7 (2*d*, C(19), C(23)); 132.9, 133.0 (2*d*, C(8)); 134.3, 134.8 (2*d*, C(12)); 139.0, 139.2 (2*s*, C(18)); 149.0 (*s*, C(21)); 150.1, 151.0 (2*d*, C(3)); 167.2 (*s*, C(11)). The mixture **59** was dissolved in MeOH (5 ml) and hydrogenated over 10% Pd/C (200 mg) in the usual way to yield a crude product (45 mg). Purification by prep. TLC (benzene/Et_2O 1:1, 2 developments) gave **60** as a white powder (19 mg) identical with **60** obtained from **40** [3]. ^{13}C-NMR: 11.4 (*q*, C(10)); 19.0 (*t*, C(8)); 25.2, 29.9, 30.2, 31.2, 34.2, 35.8 (6*t*, C(6), C(12), C(13), C(14), C(16), C(17)); 27.2 (*d*, C(5)); 29.1 (*t*, C(7)); 40.5 (*d*, C(9)); 51.2 (*q*, $COOCH_3$); 73.8 (*d*, C(15)); 97.0, 97.8 (2*d*, C(1), anom. C); 112.0 (*s*, C(4)); 121.5 (*d*, C(20), C(22)); 129.3 (*d*, C(19), C(23)); 139.2 (*s*, C(18)); 149.0 (*s*, C(21)); 151.3 (*d*, C(3)), 167.8 (*s*, C(11)).

30. *Tetrahydrohydrangenoside G Hexaacetate* (**61**). Compound **58** (408 mg) was hydrogenated over 10% Pd/C (500 mg) in MeOH (10 ml) in the usual way. The product was purified by prep. TLC (benzene/Et_2O 3:1, 5 developments) giving **61** (214 mg) as a white powder, $[\alpha]_D^{25} = -91.4°$ (*c* = 1.00, $CHCl_3$). UV: 227.5 (4.13), 270.0 (2.81). IR: 1765, 1715, 1635, 1220, 1070, 1040. ^{1}H-NMR: 0.96 (*t*, *J* = 6.0, CH_3(10)); 1.98–2.08 (5 OAc); 2.28 (*s*, arom. OAc); 3.66 (*s*, $COOCH_3$); 6.96–7.16 (*AA'BB'*, 4 arom. H); 7.34 (*s*, H–C(3)). Anal. calc. for $C_{41}H_{54}O_{18}$: C 58.98, H 6.52; found: C 58.89, H 6.56.

31. *Methyl 4α-[8-(p-Acetoxyphenyl)-4-oxo-5-octenyl]-3α-ethyl-3,4-dihydro-2β-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyloxy)-2H-pyran-5-carboxylate* (**62**). Neutral aluminium oxide (5 g) activated by heating at 100° for 3 min was placed in a solution of **61** (115 mg) in $CHCl_3$ (2 ml). After standing overnight, the mixture was diluted with $CHCl_3$/MeOH 1:1 (200 ml) and filtered. The filtrate was concentrated *in vacuo*. The residue (67 mg) was acetylated, then purified by prep. TLC (benzene/Et_2O 3:1, 3 developments) to give **62** (40 mg) as a white powder, $[\alpha]_D^{25} = -94.6°$ (*c* = 1.00, $CHCl_3$). UV: 227.5 (4.42), 270.0 (2.71). IR: 1760, 1710, 1670, 1635, 1220, 1070, 1040. ^{1}H-NMR: 0.96 (*t*, *J* = 6.0, CH_3(10)); 1.98–2.08 (4 OAc); 2.27 (*s*, arom. OAc); 3.68 (*s*, $COOCH_3$); 6.08 (*d*, *J* = 16.0, H–C(14)); 6.76 (*m*, H–C(15)); 7.00–7.20 (*AA'BB'*, 4 arom. H); 7.37 (*s*, H–C(3)). ^{13}C-NMR: 11.3 (*q*, C(10)); 19.0 (*t*, C(8)); 28.5 (*t*, C(7)); 30.0 (*d*, C(5), C(17)); 33.8, 34.0 (2*t*, C(6), C(16)); 40.2 (*t*, C(12)); 40.4 (*d*, C(9)); 51.2 (*q*, $COOCH_3$); 97.0, 97.8 (2*d*, C(1), arom. C); 111.4 (*s*, C(4)); 121.6 (*d*, C(20), C(22)); 129.3 (*d*, C(19), C(23)); 130.8 (*d*, C(14)); 138.3 (*s*, C(18)); 145.7 (*d*, C(15)); 149.2 (*s*, C(21)); 151.6 (*d*, C(3)); 167.7 (*s*, C(11)); 200.1 (*s*, C(13)). Anal. calc. for $C_{39}H_{50}O_{16}$: C 60.46, H 6.50; found: C 60.19, H 6.62.

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