

245. Studies on Monoterpene Glucosides and Related Natural Products

Part 51¹⁾

Absolute Structures of Hydrangenosides A, B, C, D, E, F, and G. Novel Type Secoiridoid Glucosides from Two *Hydrangea* Plants²⁾

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Summary

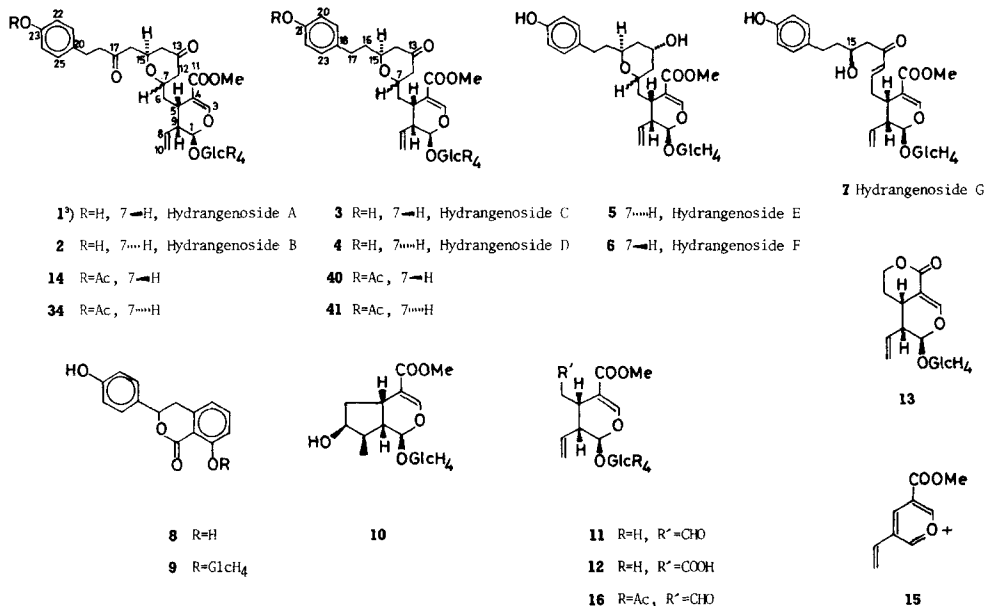
From *Hydrangea macrophylla* var. *macrophylla*, four new secoiridoid glucosides, hydrangenosides A, B, C and D, were isolated, along with the known iridoid glucosides loganin, secologanin, secologanic acid and sweroside. Moreover, hydrangenosides E, F, and G, the glucosides of the same class, were isolated 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].

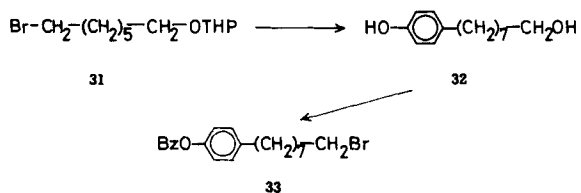
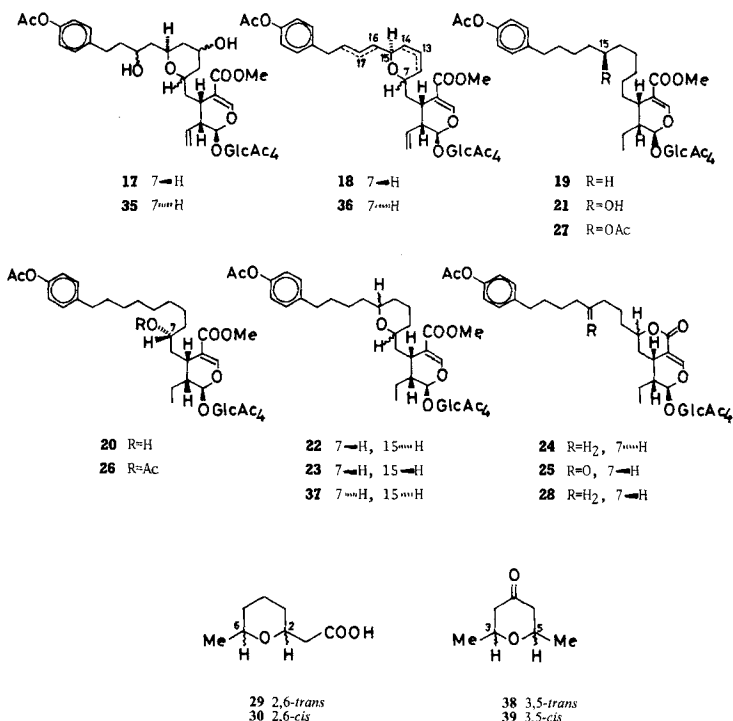
The overground parts of *H. macrophylla* var. *macrophylla* were extracted with hot H_2O , and the extract was treated with AcOEt . On concentration, AcOEt layer deposited hydrangenol glucoside (**9**). After removal of **9**, the filtrate was further concentrated and fractionated by a combination of 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].



Hydrangenoside A (**1**)³⁾, $\text{C}_{31}\text{H}_{40}\text{O}_{13} \cdot \frac{1}{2} \text{H}_2\text{O}$, $[\alpha]_D = -85.2^\circ$ (MeOH), was obtained as a white powder. Its formula was confirmed by fast-atom-bombardment (FAB) MS (m/z 621 ($(M + \text{H})^+$), 643 ($(M + \text{Na})^+$)). The spectral data (UV, IR, ^1H - 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** ($\rightarrow$ **26**, **27**); lactonization of **20** ($\rightarrow$ **28**); synthesis of **24** and **28**).

Compound **19**, $\text{C}_{41}\text{H}_{58}\text{O}_{15}$, showed signals for 9 CH_2 -groups at δ 1.24 and a COOMe -group at δ 3.66 in the ^1H -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 $\text{C}_{41}\text{H}_{58}\text{O}_{16} \cdot \text{H}_2\text{O}$, showed ^1H -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 $\text{C}(11)\text{OOMe}$ 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 $\text{C}(11)\text{OOMe}$ 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 1H -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 1H -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 1H -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 1H -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*-benzyloxypheyl)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**), $C_{31}H_{40}O_{13} \cdot H_2O$, $[\alpha]_D = -80.9^\circ$ (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 1H - 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 1H -NMR analyses.

In the 1H -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*-configured 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** $\rightarrow$ **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].

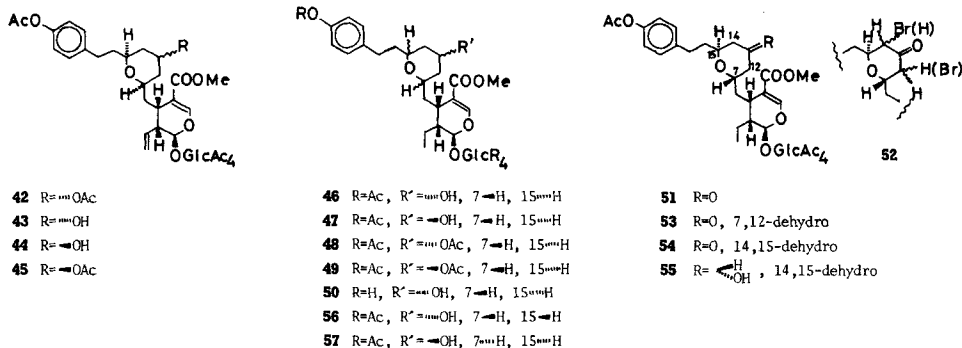
From the evidence obtained so far, it was concluded that the orientation of the C(7) and C(15) substituents of **14** and **34** are *trans* and *cis*, respectively. Since the respective C(7) configurations of **14** and **34** are (*S*) and (*R*) (*vide supra*), the C(15) of both compounds should be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

Hydrangenoside C (**3**), $C_{29}H_{38}O_{12} \cdot H_2O$, $[\alpha]_D = -94.7^\circ$ (MeOH), was obtained as a white powder, whereas hydrangenoside D (**4**), $C_{29}H_{38}O_{12} \cdot H_2O$, $[\alpha]_D = -126.3^\circ$ (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 glucosides⁴⁾, only *H. scandens* gave new type glucosides, i.e. hydrangenosides C (**3**), D (**4**), E (**5**), F (**6**), and G (**7**).

Hydrangenoside E (**5**), $C_{29}H_{40}O_{12} \cdot H_2O$, $[\alpha]_D = -108.7^\circ$ (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.



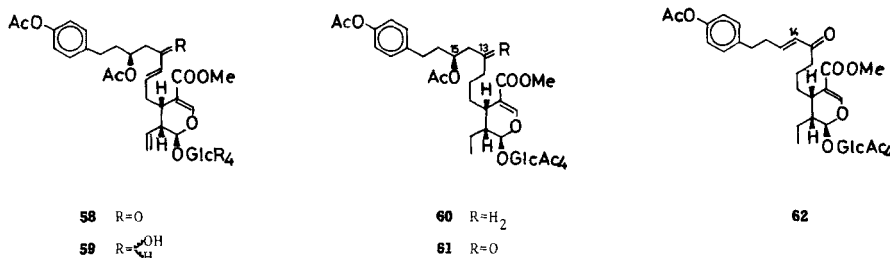
[4]. Thus, the acetate **41** of **4** was reduced with NaBH_4 to give a pair of 13-epimeric alcohols **43** and **44** in a ratio of 1:8, which on acetylation yielded the corresponding acetates **42** and **45**. Of these acetates, the minor product **42** was identical with the hexaacetate of hydrangenoside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

Hydrangenoside F (**6**), $\text{C}_{29}\text{H}_{40}\text{O}_{12} \cdot 2\text{H}_2\text{O}$, $[\alpha]_{\text{D}} = -87.0^\circ$ (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** ($\text{C}_{39}\text{H}_{47}\text{BrO}_{17}$); 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 $\text{C}_{39}\text{H}_{46}\text{O}_{17}$), 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 ($\text{C}_{39}\text{H}_{50}\text{O}_{17}$; 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.



Hydrangenoside G (**7**), C₂₉H₃₈O₁₂ · H₂O, [α]_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 G⁵⁾ has the structure **7** [4]. This was verified by chemical modifications: NaBH₄ 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 accommodated to the (*S*)-configured C(15) and the C(13), respectively.

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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 *Yanagimoto* micromelting point apparatus and are uncorrected. Optical rotations were measured with a *Jasco-DIP-180* automatic digital polarimeter. UV spectra were recorded on a *Hitachi-EP-3* or model 200-20 spectrophotometer in MeOH ($\lambda_{\max}$ in nm, $\log \varepsilon$ in parenthesis) and IR spectra on a *Hitachi-EPI-S* spectrometer or a *Shimadzu-IR-27G* grating infrared spectrometer (absorption maxima in cm^{-1}). $^1\text{H-NMR}$ spectra were recorded on *Varian-HA-100* spectrometer of *Jeol-JMN-PS-100* spectrometer, while $^{13}\text{C-NMR}$ 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 $230^\circ/\text{l} \times 10^{-7}$ 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 *PF₂₅₄* (*Merck*) was used for medium-pressure column chromatography. TLC was carried out on silica gel 60 *GF₂₅₄* or 'DC-Alufolien' silica gel 60 *F₂₅₄* (*Merck*) and prep. TLC on silica gel 60 *PF₂₅₄*, silica gel *PF₂₅₄* or 'DC-Fertigplatten' silica gel *F₂₅₄*; detection by UV irradiation or by I_2 vapour. Bands were scraped off and extracted with $\text{CHCl}_3/\text{MeOH}$ 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 $\text{H}_2\text{O}/\text{MeOH}$ 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 $\text{MeOH}/\text{CHCl}_3$ with increasing MeOH contents. The 1–2, 3–5, and 7% $\text{MeOH}/\text{CHCl}_3$ 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 ($\text{CHCl}_3/\text{MeOH}$ 85:15, 5 developments) to give secologanin acid (**12**; 9 mg). *Chrom-2* was subjected to prep. TLC ($\text{CHCl}_3/\text{MeOH}$ 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 ($\text{CHCl}_3/\text{MeOH}$ 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. $167\text{--}168^\circ$, whereas **10** gave the pentaacetate as colourless needles, m.p. $138\text{--}140^\circ$.

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. $189\text{--}191^\circ$. 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 $\text{MeOH}/\text{CHCl}_3$ with increasing MeOH contents. A 5-l fraction for each 1% of MeOH raise was collected. The eluate with 10% $\text{MeOH}/\text{CHCl}_3$ 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. $\times$ 140 cm, *Teflon* tubes, 1.4 mm i.d. $\times$ 140 cm; solvent: $\text{CHCl}_3/\text{benzene}/\text{MeOH}/\text{H}_2\text{O}$ 15:15:23:7, descending method); collecting 7-ml fractions. The residue (43 mg) of *Fractions* 421–470 was subjected to prep. TLC ($\text{CHCl}_3/\text{MeOH}$ 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. $186\text{--}187^\circ$. The residue (412 mg) of *Fractions* 471–610 was subjected to HPLC (*Bondapak C₁₈*; 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 3 α -Ethenyl-2 β -(β -D-glucopyranosyloxy)-3,4-dihydro-4 α -{[3,4,5,6-tetrahydro-6 β -[4-(p-hydroxyphenyl)-2-oxobutyl]-4-oxo-2H-pyran-2 α -yl]methyl}-2H-pyran-5-carboxylate*; **1**). White powder; $[\alpha]_D^{20} = -85.2^\circ$ ($c = 1.00$, MeOH). UV: 226.0 (4.10), 238.0 (sh, 4.04), 276.0 (sh, 2.82). IR: 3400, 1710, 1630, 1600, 1520, 1070. $^1\text{H-NMR}$: 2.10–3.00 (m , $\text{CH}_2(12)$, $\text{CH}_2(14)$, $\text{CH}_2(16)$); 2.80 (br. s , $\text{CH}_2(18)$, $\text{CH}_2(19)$); 3.68 (s , COOCH_3); 6.62–7.10 ($AA'BB'$, 4 arom. H); 7.47 (s , H–C(3)). $^{13}\text{C-NMR}$: 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*, COOCH₃); 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 C₃₁H₄₀O₁₃ · ½H₂O: C 59.13, H 6.56; found: C 59.53, H 6.71.

Hydrangenoside B (= 7-Epihydrangenoside A; 2). White powder, [α]_D²⁵ = –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. ¹H-NMR: 1.72 (*m*, CH₂(6)); 2.78 (*br. s*, CH₂(18), CH₂(19)); 3.67 (*s*, COOCH₃); 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 C₃₁H₄₀O₁₃ · H₂O: 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-2H-pyran-2α-yl]methyl}-2H-pyran-5-carboxylate; 3). White powder, [α]_D²⁵ = –94.7° (*c* = 1.12, MeOH). UV: 227.0 (4.21), 280.0 (3.24). IR: 3400, 1710, 1690, 1630, 1515, 1290, 1075, 1080, 1040. ¹H-NMR: 1.78 (*m*, CH₂(6)); 3.68 (*s*, COOCH₃); 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 C₂₉H₃₈O₁₂ · H₂O: 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°, [α]_D²⁵ = –126.3° (*c* = 1.05, MeOH). UV: 227.0 (4.27), 278.0 (3.22). IR: 3520, 3420, 1690, 1635, 1515, 1290, 1075, 1035. ¹H-NMR: 2.70 (*m*, CH₂(12), CH₂(14)); 3.68 (*s*, COOCH₃); 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 C₂₉H₃₈O₁₂ · H₂O: C 58.38, H 6.76; found: C 58.57, H 6.88.

3. Hydrangenoside A Pentaacetate (14). White powder, [α]_D²⁵ = –79.3° (*c* = 1.00, CHCl₃). UV: 222.5 (4.01). IR: 1760, 1715, 1635, 1220, 1040. ¹H-NMR: 1.72 (*br. t*, *J* = 5.5, CH₂(6)); 1.91–2.05 (4 OAc); 2.27 (*s*, arom. OAc); 2.85 (*br. s*, CH₂(18), CH₂(19)); 3.68 (*s*, COOCH₃); 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)). ¹³C-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*, COOCH₃); 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 (*OGlcAc₄), 165 (15). Anal. calc. for C₄₁H₅₀O₁₈ · ½H₂O: C 58.49, H 6.35; found: C 58.53, H 6.36.

4. Hydrangenoside B Pentaacetate (34). White powder, [α]_D²⁵ = –79.3° (*c* = 1.00, CHCl₃). UV: 220.0 (4.12). IR: 1760, 1720, 1630, 1220, 1080, 1040. ¹H-NMR: 1.36 (*m*, H–C(6)); 1.89–2.02 (4 OAc); 2.27 (*s*, arom. OAc); 2.92 (*br. s*, CH₂(18), CH₂(19)); 3.68 (*s*, COOCH₃); 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)). ¹³C-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*, COOCH₃); 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 C₄₁H₅₀O₁₈: 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-2H-pyran-2α-yl]methyl}-3α-ethenyl-3,4-dihydro-2β-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyloxy)-2H-pyran-5-carboxylate) and **Diol 35** (= 7-Epi-17). A solution of NaBH₄ (0.55 g) in H₂O (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 CHCl₃ and the CHCl₃-soluble portion washed successively with 5% HCl, H₂O, 5% NaHCO₃, and H₂O, dried, and evaporated to furnish 17 (4.80 g) as a white powder, [α]_D²⁵ = –112.7° (*c* = 1.00, CHCl₃). UV: 221.0 (4.13), 271.0 (2.91). IR: 3500, 1760, 1710, 1630, 1370, 1220, 1070, 1040. ¹H-NMR: 1.95–2.05 (4 OAc); 2.27 (*s*, arom. OAc); 3.72 (*s*, COOCH₃); 6.98–7.25 (*AA'BB'*, 4 arom. H); 7.35 (*s*, H–C(3)). Anal. calc. for C₄₁H₅₄O₁₈: 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, [α]_D²⁵ = –83.3° (*c* = 1.00, CHCl₃). UV: 213.0 (4.04), 219.0 (4.11), 271.0 (2.78). IR: 3480, 1765, 1715, 1510, 1225, 1080, 1040. ¹H-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*, COOCH₃); 6.95–7.20 (*AA'BB'*, 4 arom. H); 7.32 (*s*, H–C(3)). Anal. calc. for C₄₁H₅₄O₁₈: C 58.99, H 6.52; found: C 58.86, H 6.59.

6. Olefin 18 (= Methyl 4α-{[6β-[4-(*p*-Acetoxyphenyl)butenyl]dihydro-2H-pyran-2α-yl]methyl}-3α-ethenyl-3,4-dihydro-2β-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyloxy)-2H-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 H₂O, allowed to stand for 1 h, and extracted with CHCl₃. The CHCl₃ layer was washed successively with H₂O, 5% HCl, H₂O, 5% NaHCO₃, and

H₂O, 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 N₂. After removal of the base *in vacuo*, the residue was taken up in CHCl₃, and the CHCl₃-soluble portion was washed successively with H₂O, 5% HCl, H₂O, 5% NaHCO₃, and H₂O, dried, and concentrated *in vacuo*. The residue (3.60 g) was purified by prep. TLC (Et₂O) to furnish **18** (2.88 g) as a white powder, $[\alpha]_D^{25} = -75.7^\circ$ ($c = 1.00$, CHCl₃). UV: 210.0 (4.13), 220.0 (4.17). IR: 1760, 1710, 1630, 1370, 1070, 1040. ¹H-NMR: 1.93–2.02 (4 OAc); 2.27 (s, arom. OAc); 3.68 (s, COOCH₃); 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 C₄₁H₅₀O₁₆: 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, $[\alpha]_D^{26} = -81.4^\circ$ ($c = 0.50$, CHCl₃). UV: 213.0 (4.07), 220.5 (4.15), 270.5 (2.95). IR: 1765, 1715, 1630, 1220, 1080, 1040. ¹H-NMR: 1.94–2.05 (4 OAc); 2.27 (s, arom. OAc); 3.38 (m, H–C(7), H–C(15)); 3.67 (s, COOCH₃); 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 C₄₁H₅₀O₁₆: 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% Et₂O/benzene, and 20% Et₂O/benzene (each 500 ml, *Fractions 1–3*) and subsequently with 25% Et₂O/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 (Et₂O/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 Et₂O/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, $[\alpha]_D^{25} = -100.0^\circ$ ($c = 0.95$, CHCl₃). UV: 220.0 (4.10), 229.5 (4.11). IR: 1760, 1710, 1635, 1370, 1220, 1070, 1040. ¹H-NMR: 1.24 (br. s, 9 CH₂); 1.99–2.06 (4 OAc); 2.26 (s, arom. OAc); 2.56 (t, $J = 8.0$, CH₂(19)); 3.66 (s, COOCH₃); 6.94–7.18 (AA'BB', 4 arom. H); 7.32 (s, H–C(3)). MS (EI): 790 (M^+), 331 (⁺OGlcAc₄). Anal. calc. for C₄₁H₅₈O₁₅: 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)-2H-pyran-5-carboxylate (20). Colourless oil, $[\alpha]_D^{28} = -105.3^\circ$ ($c = 0.51$, CHCl₃). UV: 220.0 (4.08), 233.0 (4.11), 270.0 (2.82). IR: 3500, 1760, 1635, 1225, 1070, 1045. ¹H-NMR: 1.10–1.80 (m, 9 CH₂); 2.00–2.07 (4 OAc); 2.27 (s, arom. OAc); 2.58 (t, $J = 8.0$, CH₂(19)); 3.32 (m, H–C(7)); 3.74 (s, COOCH₃); 6.96–7.17 (AA'BB', 4 arom. H); 7.50 (s, H–C(3)). ¹³C-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 (8t, C(12), C(13), C(14), C(15), C(16), C(17), C(18), C(19)); 41.3 (d, C(9)); 51.8 (q, COOCH₃); 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 C₄₁H₅₈O₁₆·H₂O: 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)-2H-pyran-5-carboxylate (21). White powder, $[\alpha]_D^{22} = -81.2^\circ$ ($c = 0.70$, CHCl₃). UV: 227.0 (4.38). IR: 3500, 1760, 1710, 1630, 1370, 1220, 1070, 1040. ¹H-NMR: 0.94 (t, $J = 8.0$, CH₃(10)); 1.10–1.80 (m, 9 CH₂); 1.98–2.08 (4 OAc); 2.28 (s, arom. OAc); 2.58 (t, $J = 8.0$, CH₂(19)); 3.68 (s, COOCH₃); 3.44–3.84 (m, H–C(15)), 6.94–7.16 (AA'BB', 4 arom. H); 7.33 (s, H–C(3)). ¹³C-NMR: 11.4 (q, C(10)); 19.0 (t, C(8)); 25.3, 25.5 (2t, C(6), C(7)); 27.2 (d, C(5)); 29.0, 29.9, 30.0, 31.5, 35.3, 37.3, 37.5 (7t, C(12), C(13), C(14), C(16), C(17), C(18), C(19)); 40.5 (d, C(9)); 51.2 (q, COOCH₃); 71.6 (d, C(15)); 96.9, 97.8 (2d, 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 C₄₁H₅₈O₁₆·H₂O: 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-2H-pyran-2α-yl]methyl]-3α-ethyl-3,4-dihydro-2β-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyloxy)-2H-pyran-5-carboxylate). White powder, $[\alpha]_D^{25} = -98.0^\circ$ ($c = 0.97$, CHCl₃). UV: 220.0 (4.03), 228.5 (4.03). IR: 1760, 1710, 1630, 1370, 1220, 1070, 1040. ¹H-NMR: 0.95 (t, $J = 7.0$, CH₃(10)); 1.10–1.80 (m, 8 CH₂); 1.97–2.05 (4 OAc); 2.26 (s, arom. OAc); 2.61 (t, $J = 8.0$, CH₂(19)); 3.68 (s, COOCH₃); 3.72 (m, H–C(7), H–C(15)); 6.95–7.16 (AA'BB', 4 arom. H); 7.30 (s, H–C(3)). ¹³C-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 (6t, C(12), C(14), C(16), C(17), C(18), C(19)); 40.5 (d, C(9)); 51.2 (q, COOCH₃); 69.0, 71.1 (2d, C(7), C(15)); 96.7, 97.4 (2d, 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 (+OGlcAc₄). Anal. calc. for C₄₁H₅₆O₁₆: C 61.18, H 7.01; found: C 60.96, H 7.10.

cis-Tetrahydropyran **23** (= *cis*-Isomer of **22**). White powder, $[\alpha]_D^{25} = -71.5^\circ$ ($c = 0.94$, CHCl₃). UV: 220.0 (4.09), 229.0 (4.10). IR: 1760, 1710, 1630, 1220, 1075, 1045. ¹H-NMR: 1.10–1.80 (m, 9 CH₂); 1.93 (t, $J = 6.0$, CH₃(10)); 1.99–2.06 (4 OAc); 2.26 (s, arom. OAc); 2.58 (t, $J = 7.0$, CH₂(19)); 3.20 (m, H–C(7), H–C(15)); 3.65 (s, COOCH₃); 6.92–7.14 (AA'BB', 4 arom. H); 7.31 (s, H–C(3)). ¹³C-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 (6t, C(12), C(14), C(16), C(17), C(18), C(19)); 40.8 (d, C(9)); 51.2 (q, COOCH₃); 75.6, 77.5 (2d, 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 C₄₁H₅₆O₁₆: C 61.18, H 7.01; found: C 60.98, H 6.95.

(7*R*)-Lactone **24** (= 3β-[8-(*p*-Acetoxyphenyl)octyl]-5α-ethyl-4,4αβ,5,6-tetrahydro-6β-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyloxy)-1*H*,3*H*-pyranof[3,4-*c*]pyran-1-one). White powder, $[\alpha]_D^{25} = -75.7^\circ$ ($c = 1.01$, CHCl₃). UV: 210.0 (3.98), 219.0 (3.99), 240.0 (3.95). IR: 1760, 1710, 1630, 1375, 1220, 1065, 1045. ¹H-NMR: 1.33 (br. s, 7 CH₂); 1.94–2.07 (4 OAc); 2.26 (s, arom. OAc); 2.59 (t, $J = 8.0$, CH₂(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 C₄₀H₅₄O₁₅: C 62.00, H 7.02; found: C 62.32, H 7.25.

3α-[8-(*p*-Acetoxyphenyl)-4-oxooctyl]-5α-ethyl-4,4αβ,5,6-tetrahydro-6β-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyloxy)-1*H*,3*H*-pyranof[3,4-*c*]pyran-1-one (**25**). White powder, $[\alpha]_D^{25} = -90.8^\circ$ ($c = 1.03$, CHCl₃). UV: 210.0 (4.22), 219.0 (4.26), 227.0 (4.29), 238.0 (4.24). IR: 1760, 1710, 1625, 1220, 1060, 1040. ¹H-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)). ¹³C-NMR: 11.8 (q, C(10)); 17.5 (t, C(8)); 19.0, 23.3 (2t, C(12), C(13)); 28.2 (d, C(5)); 29.5, 30.9, 35.0, 35.2 (4t, C(6), C(17), C(18), C(19)); 37.6 (d, C(9)); 42.1, 42.4 (2t, 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 C₄₀H₅₂O₁₆: C 60.90, H 6.64; found: C 61.18, H 6.73.

cis-Tetrahydropyran **37** (= 7-*Epi*-**22**), $[\alpha]_D^{26} = -99.9^\circ$ ($c = 0.97$, CHCl₃). UV: 220.0 (4.08), 227.5 (4.10), 270.0 (2.78). IR: 1760, 1710, 1630, 1220, 1075, 1040. ¹H-NMR: 0.94 (t, $J = 8.0$, CH₃(10)); 2.02–2.06 (4 OAc); 2.27 (s, arom. OAc); 2.60 (t, $J = 7.0$, CH₂(19)); 2.84 (m, H–C(5)); 3.20 (m, H–C(7), H–C(15)); 3.66 (s, COOCH₃); 6.94–7.06 (AA'BB', 4 arom. H); 7.36 (s, H–C(3)). ¹³C-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 (6t, C(12), C(14), C(16), C(17), C(18), C(19)); 40.8 (d, C(9)); 51.1 (q, COOCH₃); 75.6, 77.7 (2d, C(7), C(15)); 97.2, 98.2 (2d, 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 C₄₁H₅₆O₁₆: 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-β-D-glucopyranosyloxy)-2*H*-pyran-5-carboxylate (**26**). Colourless oil, $[\alpha]_D^{27} = -83.9^\circ$ ($c = 1.00$, CHCl₃). UV: 220.0 (4.10), 227.5 (4.10), 270.0 (2.80). IR: 1760, 1710, 1635, 1370, 1220, 1070, 1045. ¹H-NMR: 1.98 (t, $J = 7.0$, CH₃(10)); 1.99–2.08 (5 OAc); 2.27 (s, arom. OAc); 2.58 (t, $J = 8.0$, CH₂(19)); 3.67 (s, COOCH₃); 6.96–7.16 (AA'BB', 4 arom. H); 7.34 (s, H–C(3)). Anal. calc. for C₄₃H₆₀O₁₇: 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, $[\alpha]_D^{27} = -81.3^\circ$ ($c = 1.01$, CHCl₃). UV: 220.0 (4.06), 227.5 (4.07), 270.0 (2.76). IR: 1760, 1720, 1640, 1230, 1080, 1050. ¹H-NMR: 0.96 (t, $J = 7.0$, CH₃(10)); 2.00–2.08 (5 OAc); 2.28 (s, arom. OAc); 2.60 (t, $J = 8.0$, CH₂(19)); 3.68 (s, COOCH₃); 6.96–7.16 (AA'BB', 4 arom. H); 7.34 (s, H–C(3)). Anal. calc. for C₄₃H₆₀O₁₇: 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 H₂O (0.5 ml), the mixture was further stirred for 1 h at 50–60°, and then poured onto ice-cold H₂O (100 ml) and extracted with CHCl₃ (2 × 50 ml). The CHCl₃ layer was washed successively with 5% HCl, H₂O, 5% NaHCO₃, and H₂O, dried, and concentrated *in vacuo* to give a residue (99 mg), which was chromatographed on prep. TLC plates with benzene/Et₂O 5:1 (5 developments). A main band afforded **28** (51 mg) as a white powder, $[\alpha]_D^{26} = -114.3^\circ$ ($c = 0.81$, CHCl₃). UV: 210.0 (3.99), 218.0 (4.01), 241.0 (4.00). IR: 1760, 1710, 1630, 1370, 1220, 1065, 1040. ¹H-NMR: 1.31 (br. s, 7 CH₂); 1.95–2.08 (4 OAc); 2.26 (s, arom. OAc); 2.59 (t, $J = 8.0$, CH₂(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 C₄₀H₅₄O₁₅: 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 I₂ (0.14 g) in THF (1 ml) in a N₂ 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 H₂O (300 ml) and extracted with CHCl₃ (2 × 150 ml). The CHCl₃ layer was washed successively with H₂O, 5% HCl, and H₂O, dried, and concentrated *in vacuo*. The residue (15.1 g) was chromatographed on silica gel (360 g) with CHCl₃, 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 H₂ 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 K₂CO₃ and then concentrated *in vacuo*. The residue was taken up in AcOEt (2 × 150 ml), and the AcOEt layer was washed with H₂O, dried, and concentrated *in vacuo* to give a solid (3.28 g), which was recrystallized from CHCl₃/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. ¹H-NMR: 2.50 (br. *t*, *J* = 7.0, CH₂(8)); 2.72 (br. *s*, OH); 3.63 (br. *t*, *J* = 6.0, CH₂(1)); 6.75–7.02 (*AA'**BB'*, 4 arom. H). Anal. calc. for C₁₄H₂₂O₂: 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 Ph₃P (2.52 g) and CBr₄ (1.60 g), and the mixture was stirred for 1.5 h in a stream of N₂. Removal of the resultant Ph₃PO followed by evaporation of benzene afforded a residue (6.72 g), which was chromatographed on silica gel (70 g) with hexane and CHCl₃. The CHCl₃ eluate gave 8-(*p*-hydroxyphenyl)octyl bromide (0.91 g) as a colourless oil. This compound was treated with C₆H₅CH₂Br (1.02 g) and K₂CO₃ (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. ¹H-NMR: 2.53 (br. *t*, *J* = 7.0, CH₂(8)); 3.37 (*t*, *J* = 7.0, CH₂(1)); 5.01 (*s*, PhCH₂O), 6.87–7.08 (*AA'**BB'*, 4 arom. H); 7.37 (br. *s*, 5 arom. H). Anal. calc. for C₂₁H₂₇BrO: 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 Tetraacetate (**16**). A solution of **33** (224 mg) in THF (5 ml) was added dropwise to a suspension of Mg (20 mg) and I₂ (10 mg) in THF (0.5 ml) at r.t., and the mixture was stirred for 30 min at 80° in a stream of N₂. 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 H₂O (50 ml), and extracted with CHCl₃ (2 × 50 ml). The CHCl₃ layer was washed with H₂O, dried, and concentrated *in vacuo* to give a residue (539 mg), which was subjected to prep. TLC (CHCl₃/Et₂O, 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/Et₂O 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., ¹H-NMR, IR, etc.).

14. Hydrangenoside C Pentaacetate (**40**). White powder, $[\alpha]_D^{25} = -92.8^\circ$ (*c* = 1.05, CHCl₃). UV: 220.0 (4.12). IR: 1760, 1710, 1630, 1370, 1220, 1075, 1040. ¹H-NMR: 1.88–2.07 (4 OAc); 2.26 (*s*, arom. OAc); 3.68 (*s*, COOCH₃); 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)). ¹³C-NMR: 27.5 (*d*, C(5)); 30.8 (*t*, C(17)); 34.4, 35.1 (2*r*, C(6), C(16)); 44.1 (*d*, C(9)); 46.7, 47.0 (2*r*, C(12), C(14)); 51.2 (*q*, COOCH₃); 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 C₃₉H₄₈O₁₇·H₂O: 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°, $[\alpha]_D^{25} = -104.0^\circ$ (*c* = 1.06, CHCl₃). UV: 219.5 (4.42). IR: 1760, 1715, 1630, 1510, 1370, 1220, 1070, 1040. ¹H-NMR: 1.34 (*m*, CH₂(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)). ¹³C-NMR: 25.5 (*d*, C(5)); 30.4 (*t*, C(17)); 34.0, 37.1 (2*r*, 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*, COOCH₃); 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 (⁺OGlcAc₄), 165 (**15**). Anal. calc. for C₃₉H₄₈O₁₇: 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/CHCl₃ with increasing MeOH contents. The 12, 13, 18, and 19% MeOH/CHCl₃ 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/cm²). Elution with 10% MeOH/CHCl₃ 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/CHCl₃ with increasing MeOH contents. The 16% MeOH/CHCl₃ 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/cm²). Elution with 10% MeOH/CHCl₃ 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/CHCl₃ with increasing MeOH contents. The 20% MeOH/CHCl₃ eluate furnished hydrangenoside F (**6**) (7.00 g).

Hydrangenoside E (= *Methyl 3 α -Ethenyl-2 β -(β -D-glucopyranosyloxy)-3,4-dihydro-4 α -[3,4,5,6-tetrahydro-4 α -hydroxy-6 β -[2-(p-hydroxyphenyl)ethyl]-2H-pyran-2 β -yl]methyl]-2H-pyran-5-carboxylate; **5**). $[\alpha]_D^{25} = -108.7^\circ$ ($c = 0.63$, MeOH). UV: 225.0 (4.12), 277.5 (3.20), 285.0 (3.11). IR: 3400, 1690, 1625, 1520, 1080. ¹H-NMR: 1.48 (*m*, CH₂(6), CH₂(12), CH₂(14), CH₂(16)); 2.62 (*t*, $J = 7.0$, CH₂(17)); 3.64 (*s*, COOCH₃); 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)). ¹³C-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*, COOCH₃); 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 C₂₉H₄₀O₁₂·H₂O: C 58.18, H 7.07; found: C 57.98, H 7.18.*

Hydrangenoside F (= *7-Epihydrangenoside E*; **6**). $[\alpha]_D^{25} = -87.0^\circ$ ($c = 1.00$, MeOH). UV: 226.5 (4.18), 277.5 (3.24). IR: 3400, 1690, 1630, 1515, 1290, 1080. ¹H-NMR: 1.75 (*m*, CH₂(6), CH₂(12), CH₂(14), CH₂(16)); 2.57 (*m*, CH₂(17)); 3.68 (*s*, COOCH₃); 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 C₂₉H₄₀O₁₂·2H₂O: C 56.48, H 7.19; found: C 56.76, H 7.01.

Hydrangenoside G (= *Methyl 3 α -Ethenyl-2 β -(β -D-glucopyranosyloxy)-4 α -[(6*S*)-6-hydroxy-8-(p-hydroxyphenyl)-4-oxo-2-octenyl]-2H-pyran-5-carboxylate; **7**). $[\alpha]_D^{26} = -104.1^\circ$ ($c = 1.00$, MeOH). UV: 227.0 (4.34), 278.5 (3.33). IR: 3400, 2925, 1700, 1630, 1440, 1070. ¹H-NMR: 1.68 (*m*, CH₂(16)); 2.62 (*m*, H–C(5), CH₂(6), H–C(9), CH₂(14), CH₂(17)); 3.60 (*s*, COOCH₃); 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)). ¹³C-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*, COOCH₃); 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 C₂₉H₃₈O₁₂·H₂O: C 58.38, H 6.76; found: C 58.11, H 6.92.*

17. Hydrangenoside E Hexaacetate (42). White powder, $[\alpha]_D^{25} = -95.5^\circ$ ($c = 0.99$, CHCl₃). UV: 220.0 (4.11), 270.0 (2.74). IR: 1765, 1715, 1630, 1225, 1065, 1040. ¹H-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*, COOCH₃); 7.00–7.27 (*AA'**BB'*, 4 arom. H); 7.32 (*d*, $J = 1.5$, H–C(1)). ¹³C-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*, COOCH₃); 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 C₄₁H₅₂O₁₈·½H₂O: C 58.50, H 6.35; found: C 58.31, H 6.38.

18. NaBH₄ Reduction of Hydrangenoside D Pentaacetate (41). NaBH₄ (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 CHCl₃, and the CHCl₃ layer was washed successively with H₂O, 5% HCl, H₂O, 5% NaHCO₃, and H₂O, dried, and concentrated. The residue was chromatographed on silica gel (300 g). Elution with 80% Et₂O/CHCl₃ afforded **hydrangenoside E pentaacetate (43)**, 245 mg) and **13-epi-hydrangenoside E pentaacetate (44)**, 1839 mg). **43**: White powder, $[\alpha]_D^{25} = -99.7^\circ$ ($c = 1.00$, CHCl₃). UV: 219.5 (4.08), 271.0 (2.72). IR: 3480, 1760, 1715, 1630, 1225, 1065, 1040. ¹H-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*, COOCH₃); 6.98–7.26 (*AA'**BB'*, 4 arom. H); 7.36 (*s*, H–C(3)). ¹³C-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*, COOCH₃); 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 C₃₉H₅₀O₁₇·½H₂O: 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 (Et₂O/petroleum ether), m.p. 130–132°, $[\alpha]_D^{29} = -102.6^\circ$ ($c = 1.05$, CHCl₃). UV: 225.0 (4.14), 277.5 (3.02). IR: 3480, 1760, 1715, 1630, 1220, 1070, 1040. ¹H-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, COOCH₃); 6.98–7.22 (AA'BB', 4 arom. H); 7.31 (s, H–C(3)). ¹³C-NMR: 26.3 (d, C(5)); 30.7 (t, C(17)); 34.1, 37.1 (2t, H–C(6), H–C(16)); 41.4, 41.6 (2t, H–C(12), H–C(14)); 42.6 (d, H–C(9)); 51.2 (q, COOCH₃); 68.0 (d, H–C(13)); 72.1, 73.8 (2d, C(7), C(15)); 95.8, 96.5 (2d, 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 C₃₉H₅₀O₁₇·H₂O: 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°, $[\alpha]_D^{31} = -96.2^\circ$ ($c = 0.94$, CHCl₃). UV: 225.0 (4.14), 277.5 (2.97). IR: 1765, 1715, 1630, 1220, 1075, 1045. ¹H-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, COOCH₃); 6.98–7.23 (AA'BB', 4 arom. H); 7.31 (d, J = 1.5, H–C(3)). Anal. calc. for C₄₁H₅₂O₁₈·½H₂O: C 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/CHCl₃ with increasing MeOH contents. The 15% MeOH/CHCl₃ 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]-2H-pyran-2α-yl]methyl}-2H-pyran-5-carboxylate; **50**) (348 mg) as a white powder, $[\alpha]_D^{31} = -137.3^\circ$ ($c = 0.99$, MeOH). UV: 228.0 (4.22), 278.0 (3.28), 285.0 (3.28). IR: 3400, 2950, 1700, 1630, 1515, 1070. ¹H-NMR: 1.00 (t, J = 7.0, CH₃(10)); 2.63 (m, CH₂(17)); 3.00 (m, H–C(5)); 3.67 (s, COOCH₃); 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 C₂₉H₄₂O₁₂·½H₂O: C 57.14, H 7.44; found: C 57.28, H 7.36.

20. *Dihydrohydrangenoside F Hexaacetate (48)*. White powder, $[\alpha]_D^{27} = -111.5^\circ$ ($c = 1.00$, CHCl₃). UV: 219.0 (4.07), 230.0 (4.10), 270.0 (2.69). IR: 1760, 1710, 1620, 1220, 1070, 1040. ¹H-NMR: 0.98 (t, J = 8.0, CH₃(10)); 1.98–2.05 (5 OAc); 2.25 (s, arom. OAc); 3.72 (s, COOCH₃); 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 C₄₁H₅₄O₁₈: 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 NaBH₄-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/CHCl₃ with increasing AcOEt contents. The 90% AcOEt/CHCl₃ eluate gave first **46** (2.17 g) and then **47** (0.87 g), both as a white powder.

Dihydrohydrangenoside F Pentaacetate (46). $[\alpha]_D^{27} = -105.0^\circ$ ($c = 1.00$, CHCl₃). UV: 219.0 (4.09), 229.5 (4.12), 270.5 (2.82). IR: 3475, 1765, 1715, 1635, 1225, 1070, 1040. ¹H-NMR: 1.00 (t, J = 6.0, CH₃(10)); 2.00–2.08 (4 OAc); 2.30 (s, arom. OAc); 3.68 (s, COOCH₃); 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 C₃₉H₅₂O₁₇: 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 Pentaacetate (47); $[\alpha]_D^{25} = -106.4^\circ$ ($c = 1.00$, CHCl₃). UV: 220.0 (4.09); 224.0 (4.09); 271.0 (2.82). IR: 3450, 1760, 1710, 1630, 1220, 1065, 1040. ¹H-NMR: 0.98 (t, J = 6.0, CH₃(10)); 2.00–2.10 (4 OAc); 2.30 (s, arom. OAc); 3.72 (s, COOCH₃); 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 C₃₉H₅₂O₁₇·½H₂O: 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, $[\alpha]_D^{29} = -101.9^\circ$ ($c = 1.12$; CHCl₃). UV: 220.0 (4.10); 228.0 (4.11); 270.0 (2.81). IR: 1760, 1630, 1220, 1070, 1040. ¹H-NMR: 0.97 (t, J = 7.0, CH₃(10)); 1.99–2.07 (4 OAc); 2.27 (s, arom. OAc); 2.69 (t, J = 8.0, CH₂(17)); 3.69 (s, COOCH₃); 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, $[\alpha]_D^{35} = -98.1^\circ$ ($c = 0.97$, CHCl₃). UV: 222.5 (4.16), 270.0 (2.85). IR: 1755, 1705, 1625, 1215, 1060, 1035. ¹H-NMR: 0.97 (t, J = 7.0, CH₃(10)); 1.97–2.07 (4 OAc); 2.27 (s, arom. OAc); 3.68 (s, COOCH₃); 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 C₃₉H₅₀O₁₇: C 59.23, H 6.37; found: C 59.05, H 6.51.

23. *Bromination of 51*. A solution of Br₂ (0.65 g) in dry CH₂Cl₂ (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% NaHCO₃ (250 ml), and extracted with CH₂Cl₂ (2 × 250 ml). The CH₂Cl₂ layer was washed with H₂O, 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. $^1\text{H-NMR}$: 1.03 (*t*, $J = 7.0$, $\text{CH}_3(10)$); 1.98–2.09 (4 OAc); 2.29 (*s*, arom. OAc); 2.86 (*m*, $\text{CH}_2(12)$, $\text{CH}_2(14)$); 3.70 (*s*, OCOCH_3); 4.13 (*m*, $\text{H-C}(7)$, $\text{H-C}(15)$); 7.02–7.28 (*AA'BB'*, 4 arom. H); 7.37 (*s*, $\text{H-C}(3)$). Anal. calc. for $\text{C}_{39}\text{H}_{47}\text{BrO}_{17}$: C 53.99, H 5.46; found: C 53.70, H 5.71.

24. Methyl 4 α -{[2 β -[2-(*p*-Acetoxyphenyl)ethyl]-3,4-dihydro-4-oxo-2H-pyran-6-yl]methyl}-3 α -ethyl-3,4-dihydro-2 β -(2,3,4,6-tetra-O-acetyl- β -D-glucopyranosyloxy)-2H-pyran-5-carboxylate (**53**) and Methyl 4 α -{[6-[2-(*p*-Acetoxyphenyl)ethyl]-3,4-dihydro-4-oxo-2H-pyran-2 α -yl]methyl}-3 α -ethyl-3,4-dihydro-2 β -(2,3,4,6-tetra-O-acetyl- β -D-glucopyranosyloxy)-2H-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% $\text{AcOEt}/\text{CHCl}_3$ furnished first **53** (270 mg) and then **54** (862 mg). **53**: White powder, $[\alpha]_D^{25} = -159.4^\circ$ ($c = 0.64$, CHCl_3). UV: 217.5 (4.11), 227.0 (4.13), 265.0 (4.18). IR: 1760, 1710, 1670, 1635, 1605, 1220, 1065, 1040. $^1\text{H-NMR}$: 0.97 (*t*, $J = 7.0$, $\text{CH}_3(10)$); 1.97–2.06 (4 OAc); 2.28 (*s*, arom. OAc); 2.83 (*t*, $J = 6.0$, $\text{CH}_2(17)$); 3.20 (*m*, $\text{H-C}(5)$); 3.66 (*s*, COOCH_3); 4.33 (*m*, $\text{H-C}(15)$); 5.27 (*s*, $\text{H-C}(12)$); 7.00–7.22 (*AA'BB'*, 4 arom. H). $^{13}\text{C-NMR}$: 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 (*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 $\text{C}_{39}\text{H}_{46}\text{O}_{17}$: C 59.54, H 6.13; found: C 59.58, H 5.89.

54: White powder, $[\alpha]_D^{25} = -145.4^\circ$ ($c = 0.83$, CHCl_3). UV: 233.0 (4.09), 263.0 (4.10). IR: 1760, 1710, 1670, 1632, 1610, 1220, 1070, 1040. $^1\text{H-NMR}$: 1.00 (*t*, $J = 7.0$, $\text{CH}_3(10)$); 2.01–2.07 (4 OAc); 2.28 (*s*, arom. OAc); 3.68 (*s*, COOCH_3); 4.28 (*m*, $\text{H-C}(7)$); 5.27 (*s*, $\text{H-C}(14)$); 6.98–7.20 (*AA'BB'*, 4 arom. H); 7.40 (*s*, $\text{H-C}(3)$). $^{13}\text{C-NMR}$: 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 $\text{C}_{39}\text{H}_{46}\text{O}_{17}$: C 59.54, H 6.13; found: C 59.25, H 6.11.

25. Methyl 4 α -{[6-[2-(*p*-Acetoxyphenyl)ethyl]-3,4-dihydro-4 α -hydroxy-2H-pyran-2 α -yl]methyl}-3 α -ethyl-3,4-dihydro-2 β -(2,3,4,6-tetra-O-acetyl- β -D-glucopyranosyloxy)-2H-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% $\text{Et}_2\text{O}/\text{CHCl}_3$ afforded **55** (210 mg) as a white powder, $[\alpha]_D^{24} = -112.7^\circ$ ($c = 0.70$, CHCl_3). UV: 217.5 (4.14), 265.0 (3.30). IR: 3460, 1758, 1705, 1630, 1220, 1062, 1038. $^1\text{H-NMR}$: 0.99 (*t*, $J = 7.0$, $\text{CH}_3(10)$); 1.99–2.07 (4 OAc); 2.26 (*s*, arom. OAc); 2.80 (*m*, $\text{H-C}(7)$); 4.48 (*m*, $\text{H-C}(13)$); 6.96–7.17 (*AA'BB'*, 4 arom. H); 7.36 (*s*, $\text{H-C}(3)$). $^{13}\text{C-NMR}$: 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 $\text{C}_{39}\text{H}_{50}\text{O}_{17}$: 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 ($\text{CHCl}_3/\text{Et}_2\text{O}$ 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). $[\alpha]_D^{24} = -109.1^\circ$ ($c = 0.49$, CHCl_3). UV: 215.0 (4.04), 226.0 (4.11), 268.0 (2.94). IR: 3450, 1760, 1710, 1630, 1220, 1070, 1040. $^1\text{H-NMR}$: 0.98 (*t*, $J = 7.0$, $\text{CH}_3(10)$); 1.98–2.06 (4 OAc); 2.26 (*s*, arom. OAc); 2.72 (*t*, $J = 7.0$, $\text{CH}_2(17)$); 3.28 (*m*, $\text{H-C}(7)$, $\text{H-C}(15)$); 3.66 (*s*, COOCH_3); 3.74 (*m*, $\text{H-C}(13)$); 6.94–7.18 (*AA'BB'*, 4 arom. H); 7.36 (*s*, $\text{H-C}(3)$). $^{13}\text{C-NMR}$: 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 $\text{C}_{39}\text{H}_{52}\text{O}_{17}$: 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, $[\alpha]_D^{29} = -102.9^\circ$ ($c = 1.00$, CHCl_3). UV: 226.0 (4.16), 279.0 (3.11). IR: 3550, 3500, 1762, 1710, 1220, 1070, 1045. $^1\text{H-NMR}$: 0.93 (*t*, $J = 7.0$, $\text{CH}_3(10)$); 1.98–2.03 (4 OAc); 2.26 (*s*, arom. OAc); 2.45 (*br. s*, $\text{OH-C}(13)$); 2.69 (*t*, $J = 8.0$, $\text{CH}_2(17)$); 3.22 (*m*, $\text{H-C}(7)$, $\text{H-C}(15)$); 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 $\text{C}_{39}\text{H}_{52}\text{O}_{17} \cdot \frac{1}{2}\text{H}_2\text{O}$: C 58.42, H 6.66; found: C 58.69, H 6.79.

28. *Hydrangenoside G Hexaacetate* (**58**). White powder, $[\alpha]_{\text{D}}^{24} = -95.1^\circ$ ($c = 1.00$, CHCl_3). UV: 227.5 (4.29). IR: 1760, 1710, 1670, 1630, 1220, 1065, 1040. ^1H -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 $\text{C}_{41}\text{H}_{50}\text{O}_{18} \cdot \text{H}_2\text{O}$: C 58.01, H 6.17; found: C 58.24, H 6.10.

29. *Methyl 4 α -[(6R)-6-Acetoxy-8-(p-acetoxyphenyl)octyl]-3 α -ethyl-3,4-dihydro-2 β -(2,3,4,6-tetra-O-acetyl- β -D-glucopyranosyloxy)-2H-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 ($\text{CHCl}_3/\text{Et}_2\text{O}$ 2:1) to afford a mixture **59** (= *methyl 4 α -[(6R)-6-acetoxy-8-(p-acetoxyphenyl)-4-hydroxy-2-octenyl]-3 α -ethyl-3,4-dihydro-2 β -(2,3,4,6-tetra-O-acetyl- β -D-glucopyranosyloxy)-2H-pyran-5-carboxylate*) of 13-epimeric alcohols (79 mg) as a white powder. ^1H -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. *Tetrahydrodrangenoside 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, $[\alpha]_{\text{D}}^{25} = -91.4^\circ$ ($c = 1.00$, CHCl_3). UV: 227.5 (4.13), 270.0 (2.81). IR: 1765, 1715, 1635, 1220, 1070, 1040. ^1H -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 $\text{C}_{41}\text{H}_{54}\text{O}_{18}$: C 58.98, H 6.52; found: C 58.89, H 6.56.

31. *Methyl 4 α -[8-(p-Acetoxyphenyl)-4-oxo-5-octenyl]-3 α -ethyl-3,4-dihydro-2 β -(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 $\text{CHCl}_3/\text{MeOH}$ 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, $[\alpha]_{\text{D}}^{25} = -94.6^\circ$ ($c = 1.00$, CHCl_3). UV: 227.5 (4.42), 270.0 (2.71). IR: 1760, 1710, 1670, 1635, 1220, 1070, 1040. ^1H -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 $\text{C}_{39}\text{H}_{50}\text{O}_{16}$: C 60.46, H 6.50; found: C 60.19, H 6.62.

REFERENCES

- [1] *S. Uesato, M. Ueda, H. Inouye, H. Kuwajima, M. Yatsuzuka & K. Takaishi*, *Phytochemistry* **23**, 2535 (1984).
- [2] *H. Inouye, Y. Takeda, S. Uesato, K. Uobe, T. Hashimoto & T. Shingu*, *Tetrahedron Lett.* **21**, 1059 (1980).
- [3] *S. Uesato, T. Hashimoto, Y. Takeda, K. Uobe & H. Inouye*, *Chem. Pharm. Bull.* **29**, 3421 (1981).
- [4] *S. Uesato, T. Hashimoto, Y. Takeda, H. Inouye, H. Taguchi & T. Endo*, *Chem. Pharm. Bull.* **30**, 4222 (1982).
- [5] *V. Plouvier*, *C.R. Hebd. Seances Acad. Sci.* **258**, 3919 (1964).
- [6] *Y. Asahina & J. Asano*, *Ber. Dtsch. Chem. Ges.* **63**, 429 (1930).
- [7] *Y. Ueno*, *Yakugaku Zasshi* **57**, 602 (1937).
- [8] *A.R. Battersby, A.R. Burnett & P.G. Parsons*, *J. Chem. Soc., Chem. Commun.* **1968**, 1280; *J. Chem. Soc. (C)* **1969**, 1187.
- [9] *J.P. Chapelle*, *Planta Med.* **29**, 268 (1976).
- [10] *H. Inouye, S. Ueda & Y. Nakamura*, *Tetrahedron Lett.* **1966**, 5229; *Chem. Pharm. Bull.* **18**, 1856 (1970).
- [11] *H. Inouye, K. Uobe, M. Hirai, Y. Masada & K. Hashimoto*, *J. Chromatogr.* **118**, 201 (1976).
- [12] *J.B. Stothers*, 'Carbon-13 NMR Spectroscopy', Academic Press, New York–San Francisco–London, 1972, p. 282.
- [13] *B. Maurer, A. Grieden & W. Thommen*, *Helv. Chim. Acta* **62**, 44 (1979).
- [14] *K. Mori*, *Tetrahedron* **30**, 3807 (1974).
- [15] *F.J. Weigert & J.D. Roberts*, *J. Am. Chem. Soc.* **92**, 1347 (1970).
- [16] *J.F. Sauvage, R.H. Baker & S.S. Hussey*, *J. Am. Chem. Soc.* **83**, 3874 (1961).