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A NOVEL TYPE SECOIRIDOID GLUCOSIDE, HYDRANGENOSIDE A FROM *HYDRANGEA MACROPHYLLA*

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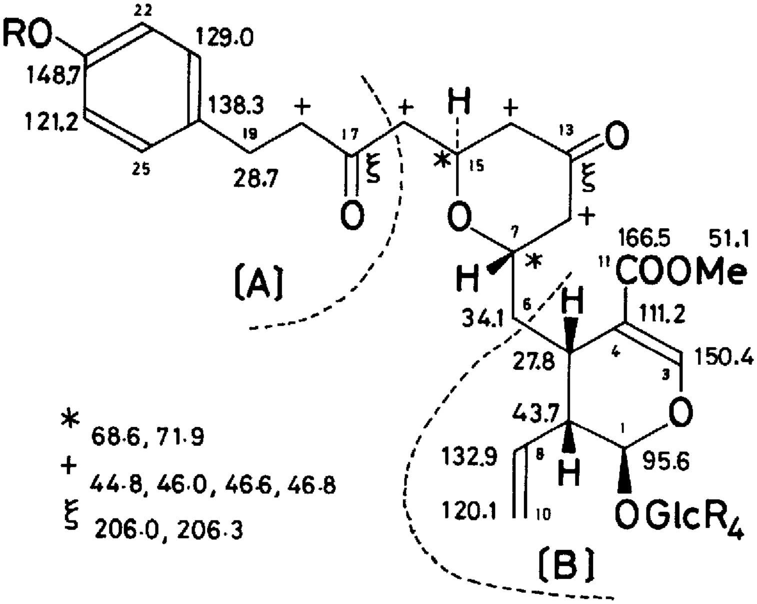
Summary: Hydrangenoside A, isolated along with its three congeners from *Hydrangea macrophylla*, was proved to have a novel type of structure which is thought to be biosynthesized through an aldol-type condensation of secologanin with a unit formed by the shikimate-malonate route followed by decarboxylation.

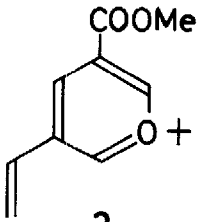
The occurrence of loganin in *Hydrangea* plants has previously been reported.$^{1)}$ The AcOEt soluble portion of the aqueous extract of *Hydrangea macrophylla* (Thunb.) Ser. var. *macrophylla* (Japanese name: Ajisai) was fractionated by a combination of silica gel column chromatography and droplet counter current chromatography,$^{2)}$ giving a series of novel type secoiridoid glucosides: hydrangenoside A, B, C and D. The remaining H_2O soluble portion, on the other hand, afforded four known glucosides of iridoid series: loganin, secologanin, secologanic acid and sweroside. In this paper, we describe the structure elucidation of hydrangenoside A, the major component among the four new glucosides.

Hydrangenoside A (1) was obtained as a white powder, $C_{31}H_{40}O_{13}\cdot 1/2\ H_2O$, $[\alpha]_D$ -85.2° (MeOH). The spectroscopic properties of 1 revealed the presence of a conjugated ester (δ_H (CD_3OD): 3.68 (s, COOMe) and 7.47 (s, 3-H); ν_{max} (KBr): 1710 and 1630 cm^{-1}) characteristic of iridoids, in addition to hydroxy groups (ν_{max}: 3400 cm^{-1}) and a *p*-substituted benzene ring (δ_H 6.62-7.10 ($A'_2B'_2$ type, H_4); ν_{max}: 1600-1520 cm^{-1}) suggesting that 1 consists of an iridoid and a non-iridoid moiety containing a *p*-substituted benzene ring. Acetylation of 1 gave a pentaacetate (2), $C_{41}H_{50}O_{18}$, whose ^1H NMR spectrum ($CDCl_3$) showed signals for a phenolic acetoxy group (δ 2.26 (s)), *p*-substituted Ph-CH_2CH_2CO- group (δ 6.93-7.23 ($A'_2B'_2$ type, H_4) and 2.85 (bs, -CH_2CH_2-)), besides frequencies of four alcoholic acetoxy groups (δ 1.91-2.05) and a conjugated ester (δ 3.68 (s, COOMe) and 7.33 (s, 3-H)). These data are indicative of the presence of the partial structure A, which is also in good agreement with the ^{13}C NMR data of 2. Furthermore, 2 showed in the mass spectrum a peak at m/e 165 (3) characteristic of secoiridoid glucosides[3] and in the ^{13}C NMR spectrum all signals corresponding to those of secologanin tetraacetate (4) except for C-6 and C-7. Therefore, 2 is presumed to have the partial structure B as the secoiridoid moiety.

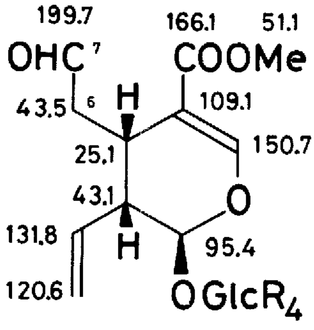
The remainder of the formula 2, $C_7H_{10}O_2$, which could not be accounted for by both partial structures A and B, was found to consist of -CO-, $-\overset{|}{C}HO\overset{|}{C}H-$ and 4 × $-CH_2-$ (three out of them linked to a carbonyl group) in view of the ^{13}C NMR and ^{1}H NMR spectra of 2. As fifteen out of the seventeen degrees of unsaturation implied by the formula 2 arise from the partial structures A and B, the remaining two could be due to a cyclic ether and a carbonyl group. On the basis of the results described above, the structures of hydrangenoside A and its pentaacetate are considered to be 1 and 2, respectively, though there remain some ambiguities regarding the stereochemistry.



1, R=H
2, R=Ac



3

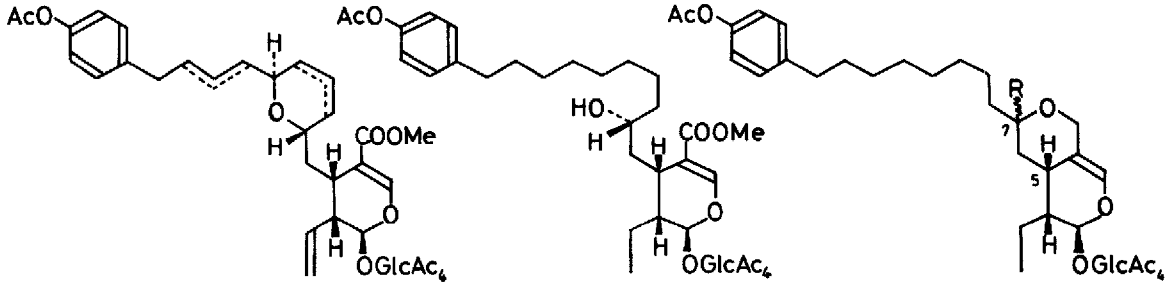


4, R=Ac
12, R=H

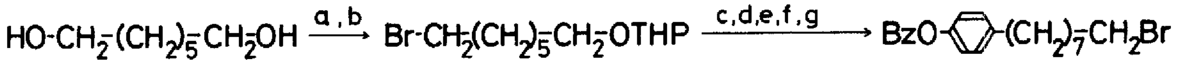
The numbers of three or four figures stand for the chemical shifts of the carbons shown in the formulae 2 and 4.
The glucose moieties of the compounds 2 and 4 also showed a similar signal pattern.

This assumption was verified by the chemical correlation described below. The acetate (2) was converted, through sequential $NaBH_4$ reduction, mesylation and demesylation, into the olefin (5) which would presumably consist of eight positional and geometrical isomers with regard to the two double bonds newly formed. Catalytic hydrogenation over Pd-C of 5 in AcOH afforded the alcohol (6), $C_{41}H_{58}O_{16}$, the lactone (7), $C_{40}H_{54}O_{15}$, and a few other compounds. The alcohol (6) on mesylation followed by treatment with H_2O furnished the 7-epilactone (8) which was formed with inversion of the configuration at C-7.

On the other hand, heptane-1,7-diol (9), when subjected to two steps of reaction (a and b), gave tetrahydropyranyloxyheptanyl bromide (10), which was further converted into *p*-benzyloxyphenyloctanyl bromide (11) through five steps of reaction (c, d, e, f and g). The bromide (11), after conversion into the organomagnesium bromide, was condensed with secologanin tetraacetate (4). The product, on catalytic reduction over Pd-C, afforded a pair of lactones in a ratio of 1 : 4; the minor one was identical with 7, whereas the major one with 8. Since the absolute structures of 7 and 8 were thus explained except for the configuration at C-7, the structure of 1 except the stereochemistry at C-7 and C-15 was also elucidated.



5 6 7, R = ---H
8, R = ◄H



HO-CH₂-(CH₂)₅-CH₂OH $\xrightarrow{a,b}$ Br-CH₂(CH₂)₅-CH₂-OTHP $\xrightarrow{c,d,e,f,g}$ BzO-⌬-(CH₂)₇-CH₂Br

9 10 11

a, HBr; b, DHP, PyH^+TsO^-; c, BzO-⌬-CHO, Mg; d, H_2/10% Pd-C; e, EtOH, PyH^+TsO^-; f, CBr_4, Ph_3P; g, BzCl, Na_2CO_3.