Reduction of Hemiacetal Ring-opened Forms of Asclepiadaceae Cardenolide Glycosides

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Reduction of gomphoside with sodium cyanoborohydride occurred with opening of the 2′-hemiacetal to yield the 3-(4,6-dideoxy-β-D-*ribo*-hexopyranoside) and the 3-(4,6-dideoxy-β-D-*arabino*-hexopyranoside) of 2α-hydroxyuzarigenin. Sodium borohydride reduction of 3′-didehydrogomphoside and 3′-*epi*-gomphoside 3′-acetate led instead to 2α-hydroxyuzarigenin 3-(4,6-dideoxy-β-D-*lyxo*-hexopyranoside). The structures of these stereoisomeric products are shown by ^{1}H and ^{13}C n.m.r. spectra. Borohydride reduction of uscharidin likewise yielded 2α,19-dihydroxyuzarigenin 3-(4,6-dideoxy-β-D-*lyxo*-hexopyranoside). In contrast, a product with an intact 2′-hemiacetal, *viz.* 19-hydroxy-3′-*epi*-gomphoside, was obtained by Reichstein *et al.* under related conditions.

An interesting feature of the cardenolide glycosides from various genera of the plant family Asclepiadaceae is the resistance of the carbohydrate group to acid hydrolysis,[1] a property related to the double linkage of carbons 1′ and 2′ of the carbohydrate (a 6-deoxyhexosulose) to the 3β and 2α positions of the aglycone through acetal and hemiacetal functions respectively.[2,3] Recently we reported the structures of several hitherto unknown glycosides from *Asclepias fruticosa*, and derived new stereochemical information on the glycosides of *Calotropis procera*.[4] In this paper we describe experiments directed towards opening of the 2′-hemiacetal function to yield products required for structure–activity relationship studies in this class of cardioactive glycosides.[5]

X-Ray analyses on gomphoside (**1a**)[6] and humistratin (**7**)[7] showed that in a crystalline state these two *Asclepias* glycosides adopt a hemiacetal structure at C-2′. Furthermore, ^{13}C n.m.r. evidence[2–4,8] indicates that a wide range of related glycosides adopt predominantly the hemiacetal form (**I**) in solution and that the alternative keto alcohol form (**II**) must contribute little, if at all, to the equilibrium (**I**) $\rightleftharpoons$ (**II**). Thus the chemical shift of the C-2′ signal of all glycosides of this class is (in $CDCl_3$, alone or in admixture with CD_3OD or CD_3SOCD_3) near δ_C 95 p.p.m., a shift in agreement with the hemiacetal form. This resonance would be expected near δ_C 200 p.p.m. for the keto alcohol form (**II**). In the case of a rapid dynamic equilibrium (**I**) $\rightleftharpoons$ (**II**), the C-2′ signal would appear significantly downfield of δ_C 95 p.p.m., the magnitude of the shift difference depending on the relative amounts of forms (**I**) and (**II**) present. Thus ^{13}C n.m.r. evidence suggests the dominance of the hemiacetal form (**I**) in gomphoside and related glycosides in the above mentioned organic solvents.

Available chemical evidence also suggests that the hemiacetal form (**I**) is predominant under some other conditions. Thus acetylation of gomphoside (**1a**), afroside (**2a**), calactin (**3a**), asclepin (**3f**), and 3′-*epi*-gomphoside 3′-acetate (**1f**) gave the corresponding acetates (**1c**), (**4c**), (**3c**) (**3g**), and (**1g**) respectively, the ^{13}C n.m.r. spectra of which show clearly that they are hemiacetal acetates.[2,4] Acetylation of the 'tertiary' hemiacetal hydroxy group at C-2′ is slow,[2] being incomplete even after 48 h at 20 °C with acetic anhydride in pyridine. It is expected that in the open keto alcohol form (**II**), the secondary alcohol on C-2 on the genin would be readily acetylated. Thus an equilibrium mixture containing even trace amounts of the open form (**II**) would produce a mixture of acetates in which those in the ring-opened form would be present in higher concentration than in the initial equilibrium mixture. There is no evidence from ^{1}H or ^{13}C n.m.r. data that the above mentioned acetylated products are in admixture with such isomers.*

However, one early observation by Reichstein indicated that the open form may be involved in some chemical transformations. Reduction of the 3′,19-dioxo glycoside uscharidin (**3d**) by sodium borohydride in 80% ethanol maintained at pH 8 was reported to give in low yield (6%) a tetrahydro derivative (**5a**) or (**5e**), characterised as the 2′,3′,19-triacetate.[9] One interesting feature of this work was the report that the corresponding 3′-alcohols calactin (**3a**) and calotropin (**3e**) on borohydride reduction gave identical dihydro derivatives (in 45 and 15% yield), which on acetylation yielded the same triacetate (**6c**).[9]† Since calactin and calotropin are epimeric at C-3′, formation of *identical* products from each by reduction (and acetylation) is difficult to rationalise on the basis of the ring-closed hemiacetal structures (**3a**) and (**3e**) respectively. If ring-opening did not take place at all, we would expect the reduction product from the 3′-ketone uscharidin (**3d**) to be 19-hydroxy-3′-*epi*-gomphoside (**5e**), formed by hydride attack on the 3′-carbonyl from the less hindered β-face with concomitant reduction of the 19-aldehyde. If calactin (**3a**) were to give the same reduction product, either epimerisation at C-3′, an unlikely event under mild basic conditions, or ring-opening followed by reversible isomerisation would have to take place.

Below we describe our studies on reactions of gomphoside (**1a**) and its 3′-epimeric analogues which proceed *via* ring-opened keto alcohol intermediates. The reduction of gomphoside by metal hydrides was studied first. Gomphoside (**1a**) was inert to sodium borohydride in ethanol, but when the reaction mixture, containing a ten-fold excess of sodium borohydride and mannitol (as a borate scavenger), was buffered by small frequent additions of benzoic acid, two products were formed very slowly. The inertness of gomphoside to borohydride reduction is not difficult to rationalise. The hemiacetal form (**I**) which is stabilised by internal hydrogen-bonding between the C-2′ and C-3′ hydroxy groups is expected to be stable under the slightly basic conditions of the reduction. Also the *cis*-diol system of

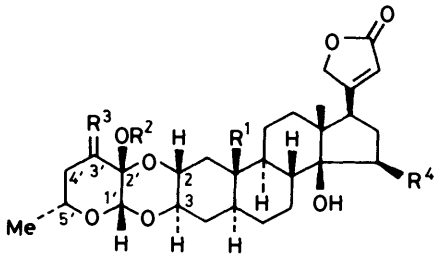
* The proposal that calotropin diacetate (**3g**) existed in the open form (B. Singh and R. P. Rastogi, *Phytochemistry*, 1972, **11**, 757) has been disproved by us.[4]

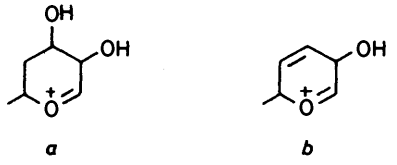
† Correctness of the ring-closed structure (**6c**) may be seen from the following parallel ^{1}H chemical shifts of gomphoside 2′,3′-diacetate (**1c**), and of Reichstein's triacetate (**6c**). Those of the 3′-epimer (**1g**) of the former are also given for comparison.

	1′-H	3′-H	6′-H
(**1c**)[2]	4.82	5.73	1.24
(**6c**)[9]	4.79	5.71	1.24
(**1g**)[4]	5.55	5.85	1.25

gomphoside (**1a**) could form a cyclic borate ester resistant to opening to the keto alcohol form (**II**).

We reasoned that these factors might be altered by reduction in acidic medium in the presence of a borate scavenger. Sodium cyanoborohydride appeared to be suitable, since its reactivity towards the reduction of ketones is enhanced under acidic conditions.[10] Furthermore, such conditions should decrease internal hydrogen-bonding and also favour opening of the C-2′ hemiacetal. Indeed, treatment of gomphoside (**1a**) with sodium cyanoborohydride in acetic acid slowly produced two products in a ratio of about 3:1. The methane chemical-ionisation (c.i.) mass spectra of the reduced products are similar and each show a quasimolecular ion at *m/z* 521, which is 2 a.m.u. higher than that of gomphoside, and dominant fragment ions *a* and *b*

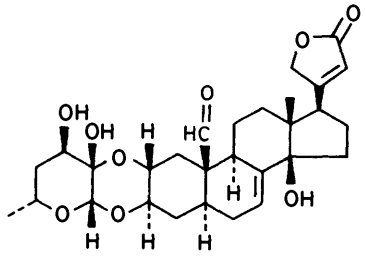




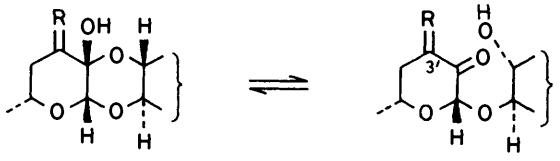
a *b*

	R^1	R^4
(1)	Me	H
(2)	Me	OH
(3)	CHO	H
(4)	Me	OAc
(5)	CH_2OH	H
(6)	CH_2OAc	H

	R^2	R^3
a;	H	β-OH, α-H
b;	H	β-OAc, α-H
c;	Ac	β-OAc, α-H
d;	H	O
e;	H	α-OH, β-H
f;	H	α-OAc, β-H
g;	Ac	α-OAc, β-H

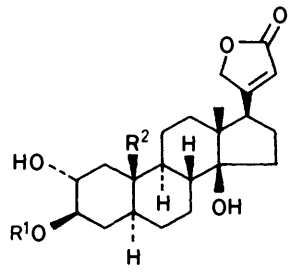


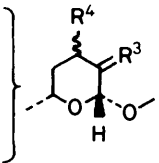
(**7**)



(**I**) (**II**)

(originating from the carbohydrate) at *m/z* 131 and 113, again 2 a.m.u. higher than the similar major fragment ions of gomphoside.[4] ^{1}H N.m.r. data (Table 1) show that the products are the epimeric alcohols (**8**) and (**9**) obtained on reduction of 2′-ketone (**10**) generated on opening of the hemiacetal. The spectra of the



	R^1	R^2	R^3	R^4
(**8**)		Me	β-OH, α-H	β-OH
(**9**)		Me	α-OH, β-H	β-OH
(**10**)		Me	O	β-OH
(**11**)		Me	α-OH, β-H	α-OH
(**12**)		CH_2OH	α-OH, β-H	α-OH
(**13**)	H	Me	–	–

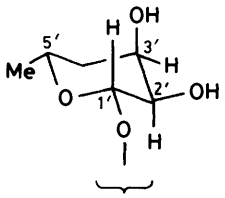
two products differ significantly only in the fact that for the major product (**9**) the signal for 1′-H is a broad singlet of half-height width ($w_{\frac{1}{2}}$) of 3 Hz at δ 4.84, whereas for the minor product (**8**), in which 1′-H and 2′-H are *trans* diaxial, 1′-H

Table 1. ^{1}H Chemical shifts (*J* and half height width $w_{\frac{1}{2}}$ in Hz)[a]

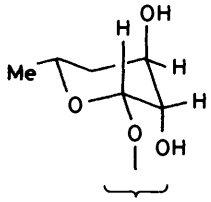
Compound	1′-H	2′-H	3′- and 2-H	3- and 5′-H	6′-H	17-H	18-H	19-H	21-H[e]	22-H[e]
(**8**)[b]	4.64d (*J* 8)	3.42dd (*J* 3 and 8)	4.0—4.4m	3.2—3.8m	1.22d (*J* 6)	2.7m	0.86	0.82	4.8 and 4.95	5.87
(**9**)[c]	4.84 ($w_{\frac{1}{2}}$ 3)	3.55d (*J* 3.5)	3.9—4.1m	3.3—3.7m	1.22d (*J* 6)	2.75m	0.85	0.81	4.85 and 5.0	5.89
(**11**)[d]	4.42 ($w_{\frac{1}{2}}$ 2)	←	3.3—3.9m	→	1.28d (*J* 6)	2.75m	0.84	0.80	4.8 and 5.0	5.86
(**12**)[c]	4.43 ($w_{\frac{1}{2}}$ 2)	←	3.3—3.9m	→	1.27d (*J* 6)	*ca.* 2.8m	0.88	*ca.* 3.75[f]	4.85 and 5.0	5.88

[a] Chemical shifts determined at 90 MHz are in p.p.m. from $SiMe_4$; d and m refer to doublet and multiplet. [b] $CDCl_3$ solvent. [c] 4:1 v/v $CDCl_3$–CD_3OD solvent. [d] 10:1 v/v $CDCl_3$–CD_3OD solvent. [e] Splitting patterns are as given in refs. 2 and 4. [f] Partially masked in this solvent but appearing as an AB quartet (*J* 11.5 Hz) in CD_3OD.

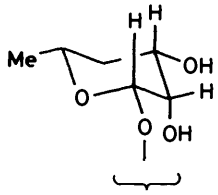
resonates as a doublet at δ 4.64 with a coupling to 2′-H of 8 Hz. The appearance of the signals for 2′-H (see Table 1) indicates that for both products $J_{2',3'}$ is *ca.* 3 Hz. With the expectation that the carbohydrates remain β at C-1′, the n.m.r. data show that the 2′-hydroxy group is axial in product (**9**) and equatorial in product (**8**) (see Figure).



(**8**)



(**9**)



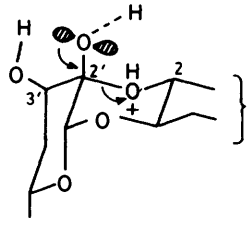
(**11**)

Figure.

In an earlier paper the isolation of a number of analogues of gomphoside from *Asclepias fruticosa* was reported.[4] In an attempt to interconvert two of these, *viz.* the 3′-ketone 3′-didehydrogomphoside (**1d**) to 3′-*epi*-gomphoside (**1e**) using sodium borohydride in methanol, we produced to our surprise the ring-opened tetrahydro derivative (**11**) in high yield. Indeed, 3′-*epi*-gomphoside (**1e**) and its 3′-acetate (**1f**) under similar conditions gave the same compound as the predominant product, reduction (and acetate hydrolysis in the case of the latter) being almost complete after 1 h. The structure of this product was indicated by the c.i. mass spectrum which was qualitatively similar to those of the reduction products of gomphoside, *viz.* compounds (**8**) and (**9**), again showing a quasimolecular ion *m/z* 521 and major fragment ions at *m/z* 131 and 113. The structure (**11**) we assign to this product corresponds to the third of four stereoisomers differing in configuration at positions 2′ and 3′. In its ^{1}H n.m.r. spectrum, a broad singlet is given by 1′-H (δ 4.42, $w_{\frac{1}{2}}$ 2 Hz).

Support for the structures of the three reduction products (**8**), (**9**), and (**11**) comes from an analysis of the ^{13}C n.m.r. data which is presented in a separate section below. Formally, the products (**8**), (**9**), and (**11**) are respectively the 3-(4,6-dideoxy-β-D-*ribo*-hexopyranoside), the 3-(4,6-dideoxy-β-D-*arabino*-hexopyranoside), and the 3-(4,6-dideoxy-β-D-*lyxo*-hexopyranoside) of 2α-hydroxyuzarigenin (gomphogenin) (**13**).

The unexpectedly rapid reduction of 3′-didehydrogomphoside (**1d**) with ring-opening to yield product (**11**) contrasts markedly with the previously reported[9] sodium borohydride reduction of uscharidin (**3d**) (which is the 19-oxo analogue) at pH 8, which gave the tetrahydro derivative (**5a**) or (**5e**) in which the hemiacetal function remained intact. We therefore investigated the sodium borohydride reduction of uscharidin in methanol (but with no pH control) and obtained the hexahydro derivative (**12**) as the predominant product in high yield. The c.i. mass spectrum of this compound showed a quasimolecular ion at *m/z* 537 which is 6 a.m.u. higher than that of uscharidin (**3d**), and major fragment ions at 131 and 113, also found in the previously discussed opened analogues (**8**), (**9**), and (**11**), attributable to ions *a* and *b* of the carbohydrate portion of the molecule. The stereochemistry of the reduction product (**12**) follows as discussed earlier from the appearance of the 1′-H resonance as a broad singlet ($w_{\frac{1}{2}}$ 2 Hz) in the ^{1}H n.m.r. spectrum (Table 1). It is thus 2α,19-dihydroxyuzarigenin 3-(4,6-dideoxy-β-D-*lyxo*-hexopyranoside) (**12**).



(III)

Table 2. ^{13}C Chemical shifts δ_C (in p.p.m.)

Carbon number	(13)[b,e]	(1a)[b]	(8)[a]	(9)[a]	(11)[c]	(12)[d]
1′	—	94.2	100.7	97.5	98.6	97.9
2′	—	90.3	71.4	69.7*	70.2*	70.2*
3′	—	70.7	67.3	68.0**	68.7	68.6
4′	—	36.6	38.4	34.8	35.5	35.5
5′	—	66.2	67.3	67.3**	68.7*	68.6*
6′	—	20.5	20.4	20.8	20.4	20.2
1	44.9	42.2	44.4	44.5	44.6	41.4
2	72.2	69.3	70.1	70.1*	70.0*	70.2
3	75.9	72.5	87.1	85.1	83.7	82.3
4	35.2	32.0	33.9	33.5	32.9**	32.8**
5	44.3	44.8	44.2	44.2	44.2	44.5
6	27.7	27.8	27.7	27.8	27.9	27.5
7	27.1	27.3	27.2	27.2	27.3	27.5
8	40.5	40.5	40.9	40.8	40.7	40.2
9	49.6	49.7	49.6	49.7	49.8	47.2
10	37.3	37.8	36.8	36.8	36.9	40.7
11	21.2	21.3	21.2	21.2	21.3	22.8
12	39.6	39.6	39.7	39.7	39.7	39.6
13	49.6	49.7	49.6	49.7	49.8	50.3
14	84.8	84.8	85.4	85.2	84.8	85.3
15	32.3	32.4	32.9	32.8	32.4**	32.3**
16	26.8	26.8	26.9	26.9	27.0	27.0
17	50.8	50.9	50.7	50.8	51.0	51.1
18	15.5	15.5	15.7	15.6	15.6	15.5
19	12.9	13.4	13.0	13.0	12.9	59.4
20	176.4	176.4	174.6	175.4	176.6	177.3
21	73.8	73.9	73.5	73.7	74.0	74.3
22	116.8	117.0	117.5	117.3	116.9	116.8
23	175.8	175.8	174.6	175.1	175.8	176.2

[a] In $CDCl_3$, with δ_C 77.1 p.p.m. [b] In 3:1 v/v $CDCl_3$–CD_3OD, with $\delta_C(CDCl_3)$ 77.3 p.p.m. [c] In 1:2 v/v $CDCl_3$–CD_3OD, with $\delta_C(CD_3OD)$ 48.3 p.p.m. [d] In 1:4 v/v $CDCl_3$–CD_3OD with $\delta_C(CD_3OD)$ 48.3 p.p.m. [e] Modified data of J. F. Templeton, H. T. A. Cheung, C. R. Sham, T. R. Watson, and Kong Jie, *J. Chem. Soc., Perkin Trans. 1*, 1983, 251.

*,** Signals within a vertical column may be interchanged.

Our reduction of both 3′-didehydrogomphoside (**1d**) and 3′-*epi*-gomphoside 3′-acetate (**1f**) obviously takes place *via* 3-*epi*-gomphoside (**1e**). The ready opening of the 2′-hemiacetal in 3′-*epi*-gomphoside (**1e**) in contrast to the situation for gomphoside (**1a**) calls for comment. One or both of two factors may contribute to the differences in reactivity. The first is one of stereoelectronic control in hydrolytic reactions.[11] The cleavage of the O–C(2′) bond is expected to be favoured when the 2′-

hydroxy group can adopt a conformation in which one of its lone pairs is oriented antiperiplanar with respect to the departing oxygen atom attached to C-2′ [*e.g.*, as in structure (**III**)]. In the case of gomphoside (**1a**), this same lone pair is, in this conformation, well aligned to participate in hydrogen-bonding to the axial 3′-hydroxy group. Modification of *X*-ray crystallographic data by computer graphics shows that in this situation the O ··· H distance is about 2.2 Å, within the range for hydrogen-bond formation.[12] With the 2′-hydroxy group in this conformation thus depleted of nonbonded electrons, the relative reluctance of gomphoside to undergo O–C(2′) cleavage can be rationalised. The same unfavourable situation does not exist for 3′-*epi*-gomphoside (**1e**) which cleaves readily. A second factor may be that after ring-opening, the product from 3′-*epi*-gomphoside, with an equatorial 3′-OH [*cf.* structure (**II**)], is more stable than that from gomphoside, in this case having an axial 3′-OH.

^{13}C *N.m.r. Data.*—The ^{13}C n.m.r. spectra of the four reduction products (**8**), (**9**), (**11**), and (**12**) are in agreement with the structures assigned. Three of the reduction products, *viz.* (**8**), (**9**), and (**11**), are 3-glycosides of the genin gomphogenin (2α-hydroxyuzarigenin) (**13**). As shown in Table 2, the chemical shifts of their aglycone carbon atoms (other than carbons 2, 3, and 4) parallel those of the corresponding carbons in gomphoside (**1a**) and in gomphogenin (**13**). Assignments of these steroids' carbons have earlier been discussed by us.[4,13] Comparison of these three isomers with their 19-hydroxy analogue (**12**) shows that the 19-hydroxy group has shielding effects on C-1 (−3 p.p.m.) and C-9 (−2.5 p.p.m.) which are γ to it. Expected α and β deshielding effects on C-19 (46.5 p.p.m.) and C-10 (4 p.p.m.) are also observed.

As shown in the Figure, reduction products (**8**), (**9**), and (**11**) differ only in the configuration at positions 2′ and 3′ of the hexose. In the following discussion, a comparison is made between the ^{13}C chemical shifts of these three products for the carbohydrate carbons, as well as for carbons 2—4 on the aglycone (the shieldings of which are influenced by the carbohydrate). The 19-alcohol (**12**) has the same carbohydrate as its 19-methyl analogue (**11**), and these compounds give rise to nearly identical shieldings for the above mentioned carbons. Thus *any reference below to product* (**11**) *applies also to its* 19-*hydroxy analogue* (**12**).

Each of the three isomeric glycosides (**8**), (**9**), and (**11**) is characterised by a methine carbon signal near δ_C 85 p.p.m., which is assigned to C-3. The same carbon in gomphogenin (**13**) resonates at δ_C 76 p.p.m. The chemical-shift changes at C-3 (*ca.* 9 p.p.m.) (as well as those of carbons 2 and 4) upon attachment of the carbohydrate (glycosidation shifts)[14] reflect the conformations at the aglycone carbon (C-3)-to-glycosidic oxygen bond, and the anomeric carbon (C-1′)-to-glycosidic oxygen bond. The predicted unequal glycosidation shifts on carbons 2 and 4 (ref. 14) may not be relevant here, as C-2 bears a hydroxy group. Nevertheless for each of the three 3-glycosides, signals 1—3 p.p.m. upfield of those for carbons 2 and 4 in gomphogenin (**13**) (72 and 35 p.p.m. respectively) may be assigned to these carbons, as small γ effects of C-1′ on these carbons are expected.

Turning to the carbohydrate carbons, the signal for C-4′ in glycoside (**9**) (δ_C 34.8 p.p.m.) is upfield of that in glycoside (**8**) (δ_C 38.4 p.p.m.). As both glycosides are derived from gomphoside (**1a**), they both possess an axial 3′β-hydroxy group, but differ in the configuration at C-2′. For C-4′ the steric γ-*gauche* shielding effect of an axial 2′β-OH in glycoside (**9**) is replaced by a periplanar heteroatom effect (also shielding)[15] of an equatorial 2′α-OH in glycoside (**8**) (see the Figure). The difference between such effects (in a number of carbohydrates) is of the order of 2.5 p.p.m.[16] The observed C-4′ shift difference (3.6 p.p.m.) thus confirms the stereochemical assignment made from ^1H n.m.r. coupling constants. Also in support is the observed C-1′ (anomeric carbon) shift difference between glycosides (**9**) (δ_C 97.5 p.p.m.) and (**8**) (δ_C 100.7 p.p.m.), which is in agreement with the presence adjacent to C-1′ of an axial 2′-hydroxy group in the former, and an equatorial one in the latter.

With one exception, signals for carbons 2′, 3′, and 5′ are found within the narrow range 68.8 ± 1.5 p.p.m., and unambiguous assignments for all of them are not given here. Comments are given below on some of the signals given by these carbons. In contrast to the other two glycosides, glycoside (**8**) bears an equatorial hydroxy group at C-2′, and a signal at δ_C 71.4 p.p.m., outside the above mentioned range, is assigned to C-2′. C-5′ In glycoside (**8**) or (**9**) is subjected to γ-*gauche* shielding by an axial 3′-OH and, particularly as it is next to C-4′ which is unsubstituted, is assigned relatively upfield signals near δ_C 67.5 p.p.m.

Experimental

For general procedures see ref. 4. Preparative and analytical h.p.l.c. separations were performed using a 1:18 v/v mixture of methanol–ethyl acetate. In assigning ions in the methane chemical-ionisation (c.i.) mass spectral data, *G* refers to the genin gomphogenin (**13**). For ^1H and ^{13}C n.m.r. data of products described in this section, see Tables 1 and 2.

Reduction of Gomphoside (**1a**) *with Sodium Cyanoborohydride.*—(*a*) Sodium cyanoborohydride (0.20 g) was added to a stirred solution of gomphoside (**1a**) (0.35 g) and mannitol (2 g) in acetic acid (40 ml). After 1 h a further quantity (0.20 g) of sodium cyanoborohydride was added, and the mixture was stirred at room temperature for 14 h. After dilution to 500 ml with water the mixture was extracted with chloroform (3 × 150 ml) and the combined extracts were dried over sodium sulphate. The residue obtained on evaporation of solvent was dissolved in the minimum volume of chloroform and separated by preparative h.p.l.c. (100 μl injections, 10 mg per injection) to give 2α-hydroxyuzarigenin 3-(4,6-dideoxy-β-D-*ribo*-hexopyranoside) (**8**) (45 mg), 2α-hydroxyuzarigen 3-(4,6-dideoxy-β-D-*arabino*-hexopyranoside) (**9**) (155 mg), and recovered gomphoside (48 mg).

(*b*) Sodium cyanoborohydride (50 mg) was added to a stirred solution of gomphoside (**1a**) (50 mg) in acetic acid (5 ml) containing mannitol (100 mg). Further additions of sodium cyanoborohydride (30 mg) and mannitol (50 mg) were made after 1 and 3 h. After being kept for a further 4 h the reaction mixture was diluted with water, worked up, and separated as above to give the reduction product (**8**) (12 mg), the product (**9**) (24 mg), and of unchanged gomphoside (5 mg).

2α-*Hydroxyuzarigenin* 3-(4,6-*dideoxy*-β-D-ribo-*hexopyranoside*) (**8**), obtained as fine crystals by slow addition of hexane to a hot solution in methanol–ethyl acetate, had m.p. 137.5—138.5 °C, *m/z* (methane c.i.) 549 (*M* + C_2H_5, 9%), 521 (*M*H$^+$, 28), 391 (*G*H, 16), 373 (391 − H_2O, 12), 355 (391 − $2H_2O$, 15), 337 (391 − $3H_2O$, 10), 131 (*a*, 75), and 113 (*b*, 100) (Found: C, 67.25; H, 8.5. $C_{29}H_{44}O_8$ requires C, 66.9; H, 8.5%).

2α-*Hydroxyuzarigenin* 3-(4,6-*dideoxy*-β-D-arabino-*hexopyranoside*) (**9**), similarly obtained as fine crystals, had m.p. 142—144 °C, *m/z* (methane c.i.) 549 (*M* + C_2H_5, 7%), 521 (*M*H$^+$, 22), 391 (*G*H, 14), 373 (391 − H_2O, 12), 355 (391 − $2H_2O$, 13), 337 (391 − $3H_2O$, 10), 131 (*a*, 48), and 113 (*b*, 100) (Found: C, 66.6; H, 8.45%).

Reduction of 3′-epi-*Gomphoside* (**1e**), *its* 3′-*Acetate* (**1f**), *and* 3′-*Didehydrogomphoside* (**1d**) *with Sodium Borohydride.*—Sodium borohydride (10 mg) was added to a solution of 3′-*epi*-gomphoside 3′-acetate (**1f**) (20 mg) in methanol (5 ml). Monitoring of the reaction mixture by t.l.c. revealed that

reduction and hydrolysis of the acetate group had proceeded concurrently. After 30 min, further sodium borohydride (5 mg) was added and the mixture was stirred for 3 h by which time a single, low R_F product was observed. The reaction mixture was diluted with water (50 ml), extracted with chloroform (3 × 10 ml), and the dried (sodium sulphate) extracts concentrated under reduced pressure to give 2α-*hydroxyuzarigenin* 3-(4,6-*dideoxy*-β-D-lyxo-*hexopyranoside*) (**11**) as a gum (18 mg) which was pure by h.p.l.c., *m/z* (methane c.i.) 521 (MH^+, 2%), 391 (*G*H, 3), 373 (391 − H_2O, 2), 355 (391 − $2H_2O$, 2), 337 (391 − $3H_2O$, 1), 159 (5), 131 (*a*, 70), and 113 (*b*, 100) (Found: C, 66.7; H, 8.55%). Reduction of 3-didehydrogomphoside (**1d**) or of 3′-*epi*-gomphoside (**1e**) by the same procedure gave, in 85% yield, the product (**11**), identical (t.l.c., ^1H and ^{13}C n.m.r.) with the sample obtained by reduction of 3′-*epi*-gomphoside 3′-acetate.

Reduction of Uscharidin (**3d**) *with Sodium Borohydride.*— Upon reduction carried out as described for the reduction of 3′-*epi*-gomphoside 3′-acetate (**1f**), uscharidin (**3d**) gave 2α,19-dihydroxyuzarigenin 3-(4,6-dideoxy-β-D-*lyxo*-hexapyranoside) (**12**), *m/z* (methane c.i.) 565 (*M* + C_2H_5, 0.4%), 537 (MH^+, 0.2), 519 (*M*H − H_2O, 0.4), 407 (*G*H, 2.0), 389 (407 − H_2O, 0.7), 371 (407 − $2H_2O$, 1.5), 353 (8), 159 (0.7), 131 (*a*, 32), and 113 (*b*, 100).

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