Cardenolide Analogues. Part 12.[1] ^{13}C N.m.r. of Semi-synthetic Glycosides and Side-chain Modified Genins

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^{13}C N.m.r. chemical shifts of a number of semi-synthetic cardenolide analogues are presented and the signal assignments justified. Compounds studied include digitoxigenin analogues having αβ-unsaturated 17β-side-chains; the α-L-rhamnopyranoside, β-D-glucopyranoside, and β-D-galactopyranoside of digitoxigenin and/or uzarigenin, and some peracetylated derivatives thereof. The effects of both structural changes in the side-chain and glycoside formation on the chemical shifts of certain carbons on the steroid skeleton are analysed.

THE technique of ^{13}C n.m.r. spectroscopy is invaluable in providing structural information on complex organic molecules. The technique is particularly convenient when the assignment of signals is facilitated by the availability of systematic data from a series of related compounds such as in the cases of steroids and carbohydrates.[2]

Systematic ^{13}C n.m.r. studies on the cardenolides have hitherto been confined to two groups of such substances both having an intact butenolide ring at C-17, *i.e.* the genins,[3] and cardenolides with a 6-deoxyhexosulose doubly linked to the aglycone at positions 2α and 3β.[4] Apart from the work of Abe and Yamauchi,[5] only isolated examples of the more common 3-glycosides [6] were examined, as were examples of genins with modified lactone rings.[7] In this paper we present a study of the ^{13}C n.m.r. spectra of two types of semi-synthetic cardenolide analogues: (*a*) pyranosides of digitoxigenin (2) (with 5β-H) and of uzarigenin (1) (with 5α-H); and (*b*) analogues of digitoxigenin in which the butenolide ring at C-17 has been replaced by an αβ-unsaturated system. The syntheses of these analogues have been reported elsewhere.[1,8]

RESULTS AND DISCUSSION

The n.m.r. data presented here include the ^{13}C chemical shifts of (*i*) genins with a butenolide or a butanolide ring (Table 1); (*ii*) genins with an αβ-unsaturated ester group at C-17 (Table 2); (*iii*) other side-chain modified genins (Table 3); (*iv*) L-rhamnopyranosides (which are 6-deoxyhexopyranosides) (Table 4); and (*v*) D-glucopyranosides and D-galactopyranosides (hexopyranosides) (Table 5).

Most cardenolide glycosides and some of the C-17 modified genins are poorly soluble in deuteriochloroform. In this work we have made extensive use of a mixture of deuteriochloroform and [$^2H_6$]dimethyl sulphoxide (1 : 2) which yields chemical-shift values which are generally within 1 p.p.m. of those recorded in deuteriochloroform (see *e.g.* Table 1, columns 2 and 3, and Table 2).† Some of the less polar genins were run in deuteriochloroform so that the ^{13}C shieldings may be easily related to the extensive literature data on steroids.[2a]

Assignments of the ^{13}C n.m.r. signals are based on chemical-shift theory, observed multiplicities in the single-frequency off-resonance decoupled (s.f.o.r.d.) spectra, internal consistency, and comparison with ^{13}C n.m.r. data in the literature on cardenolide genins and on carbohydrates which we consider as reliable. More specific discussion of the assignments follows.

TABLE 1

^{13}C Chemical shifts of genins

	Uzarigenin (1) [a,c]	Digitoxigenin (2) [d]		20(22)-Dihydrodigitoxigenin (3) [b,e]
		b	*a*	
C-1	37.0	29.6	29.6	29.6
C-2	31.2	27.8	27.7	27.8
C-3	69.7	66.7	65.0	66.8
C-4	38.0	33.1	33.2	33.2
C-5	44.3	35.9	35.8	36.0
C-6	28.6	26.4	26.6	26.4
C-7	27.3	21.2	21.2	21.1
C-8	41.0	41.6	41.1	41.4
C-9	49.5	35.3	35.1	35.3
C-10	35.5	35.3	35.1	35.3
C-11	20.9	21.2	20.9	20.8
C-12	39.3	39.9	39.4	39.5
C-13	49.5	49.6	49.6	47.0
C-14	84.0	85.4	84.0	85.7
C-15	32.3	32.9	32.2	32.0
C-16	26.6	26.9	26.6	25.5
C-17	50.6	50.9	50.6	53.8/54.0 [f]
C-18	15.7	15.7	15.7	15.7
C-19	12.1	23.7	23.8	23.7
C-20	175.6	175.3	175.9	40.8
C-21	73.2	73.6	73.2	73.9/72.4 [f]
C-22	116.7	117.3	116.6	33.2
C-23	173.8	174.9	173.9	177.7

[a] In $CDCl_3$–CD_3SOCD_3, δ($CDCl_3$) 78.8. [b] In $CDCl_3$ solution, δ 77.1. [c] For assignments in pentadeuteriopyridine see ref. 3*c*. [d] For assignments in CD_3OD–$CDCl_3$ (2 : 3) see ref. 3*a*. [e] Major and minor C-20 epimers.

Signals of Modified Digitoxigenin Analogues and of Steroid Aglycone Carbons of Glycosides.—Signals of the side-chain modified genins listed in Tables 2 and 3 and the aglycone carbon signals of the glycosides listed in Tables 4 and 5 are assigned by comparison with the ^{13}C shieldings of the 5α-genin uzarigenin (1) and the 5β

† As exceptions there are significant shift differences for carbons attached to oxygen (solvation phenomenon). Thus comparing appropriate compounds in Tables 1—3, carbons 3 and 14 are *ca.* 1.5 p.p.m. upfield in $CDCl_3$–CD_3SOCD_3 compared to deuteriochloroform.

TABLE 2

^{13}C Chemical shifts of unsaturated esters [a]

	(10) [b]	(11) [b]	(12)	(13)	(5)
C-1	29.7	29.7	29.7	29.6	29.7
C-2	27.8	27.9	27.7	27.7	27.9
C-3	66.8	66.9	65.1	65.3	66.9
C-4	33.3	33.4	33.3	33.2	33.3
C-5	36.1	36.1	35.9	35.9	36.1
C-6	26.5	26.6	26.7	26.6	26.6
C-7	21.2	21.2	21.1	21.1	21.3 *
C-8	41.9	41.9	41.1	41.2	42.0
C-9	35.5	35.5	35.1	35.1	35.6
C-10	35.5	35.5	35.1	35.1	35.4
C-11	20.8	20.8	20.6	20.6	21.0 *
C-12	38.8	38.8	38.4	38.5	39.3
C-13	49.1	49.2	49.0	48.9	49.5
C-14	85.9	85.9	84.4	84.6	86.0
C-15	32.6	32.7	32.1	32.2	32.7
C-16	26.8	26.8	26.9	26.8	27.4
C-17	54.1	54.1	54.0	54.0	51.7
C-18	15.8	15.8	16.0	15.9	15.4
C-19	23.8	23.8	23.9	23.8	23.8
C-20 [c]	155.4	155.0	156.0	155.5	148.8
C-22 [c]	119.1	119.7	118.7	119.2	125.0
C-23 [c]	167.4	167.0	166.3	165.9	169.3
O–C<	51.3	60.1	65.1	66.5	49.5
O–CH_2C<		14.3	21.9	21.8	
O–CH_2CH_2Me			10.4		
>C=CMe					12.3

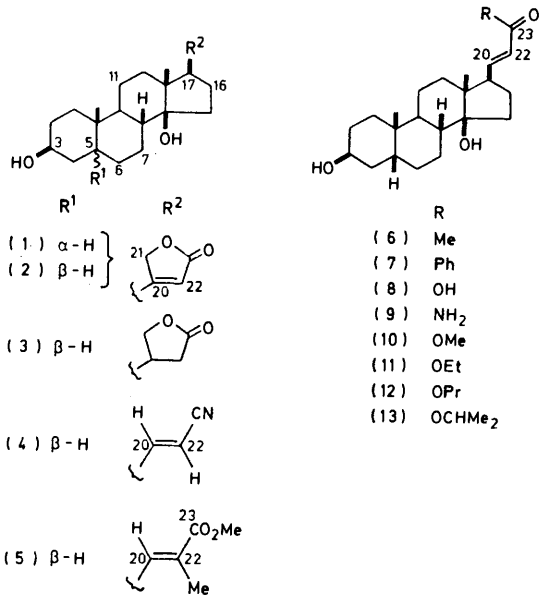
[a] In p.p.m. downfield from $SiMe_4$ in $CDCl_3$–CD_3SOCD_3, δ($CDCl_3$) 78.8 unless otherwise stated. [b] In $CDCl_3$, δ 77.1. [c] For numbering, see structures (6)—(13).

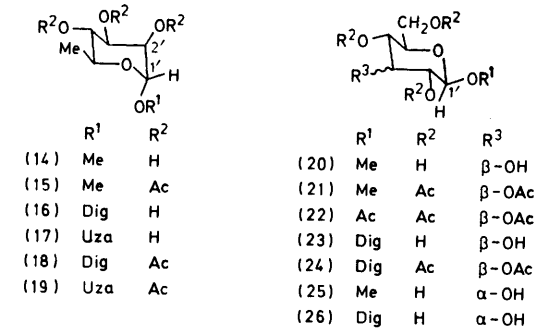
* Signals may be interchanged.

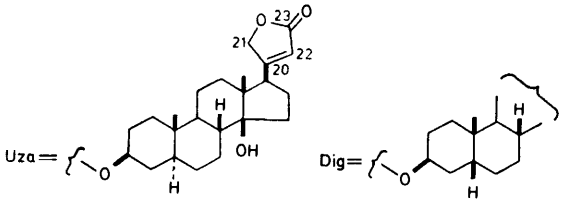
genin digitoxigenin (2) as shown in Table 1, and with the data of the corresponding 3-acetates (recorded in deuteriochloroform).[4b] The comments below refer only to non-trivial assignments of carbon signals in the same chemical-shift range.

In the spectra of uzarigenin (1), digitoxigenin (2) (Table 1), and their glycosides (Tables 4 and 5), there are two quaternary carbon signals in the range δ 174—177. The higher-field and weaker signal (near δ 174) is assigned to the carbonyl carbon (C-23) of the butenolide ring since in the s.f.o.r.d. spectra of some glycosides this signal showed sharp splitting due to a single two-bond coupling (J_{CCH}) to a proton (H-22). The signal of the vinyl carbon C-20 is expected to be subjected to more complex splitting by protons and is designated a shift of *ca.* δ 176.5. In the genins (4)—(13), the butenolide at C-17 is replaced by an enone- or enoate-type side-chain which has been given steroid numbering [see (6)—(13)] for ease of association with the butenolide ring. Signals of the α and β carbons on this αβ-unsaturated system (C-22 and C-20, respectively) are readily distinguished from one another by charge-density considerations.[9]

Comparing digitoxigenin derivatives having an intact butenolide ring (Tables 1, 4, and 5) with those modified at C-17 (Tables 2 and 3), the perturbation of the shieldings of carbons 11 and 16 by the C-17 side-chain may be discerned. This forms the basis for distinguishing between the two methylene signals near δ 21 (carbons 7 and 11) and between the three signals near δ 26 (carbons 2, 6, and 16). Thus for all 5β-H genins and glycosides in Tables 1—5, the signals of C-7 and C-6 remain within the narrow ranges of δ 21.1—21.3 and 26.4—26.7 respectively (for $CDCl_3$–CD_3SOCD_3 or deuteriochloroform solutions). Of these compounds, those with a C-17 butenolide ring [see (2), (16), (18), (23), (24), and (26) in







Tables 1, 4, and 5] give rise to C-11 and C-16 signals also within narrow ranges, *i.e.* δ 20.8—21.0 and 26.5—26.9, respectively. However, for compounds with an unbranched enone- or enoate-type chain at C-17 [see (4)—(13) in Tables 2 and 3], slightly increased shielding of C-11 (δ 20.6—20.8) and more pronounced perturbation of C-16 shieldings (δ 26.6—27.1) are observed.* A third methylene signal near δ 26 appears in the spectra of digitoxigenin glycosides [see (16), (23), and (24)]. This signal near δ 26.2 is assigned to C-2, since it is replaced by one near δ 27.7 in digitoxigenin (2) (Table 1) and other

* Compound (5) with a *branched* conjugated ester side-chain shows perturbation of C-11 (δ 21.0/21.3) and deshielding of C-16 (δ 27.4) by the C-22 methyl.

TABLE 3

^{13}C Chemical shifts of C-17 modified genins [a]

	(4)	(6)	(7) [b]	(8)	Potassium salt of (8) [c]	(9)
C-1	29.7	29.6	29.6	29.7	[29.6]	29.7
C-2	27.7	27.7	27.7	27.7	[27.5]	27.7
C-3	65.1	65.7	66.6	65.1	[65.5]	65.5
C-4	33.3	33.2	33.2	33.3	[33.2]	33.3
C-5	35.9	35.9	35.9	35.9	[36.0]	36.0
C-6	26.6	26.6	26.5	26.7	[26.7]	26.6
C-7	21.1	21.1	21.2	21.2	[21.1]	21.1
C-8	41.0	41.4	41.7	41.2	[40.8]	41.3
C-9	35.1	35.2	35.3	35.1	[35.2]	35.2
C-10	35.1	35.2	35.3	35.1	[35.2]	35.2
C-11	20.6	20.7	20.8	20.7	[20.8]	20.7
C-12	37.9	38.5	38.8	38.5	[39.1]	38.8
C-13	49.3	49.3	49.5	48.9	[48.4]	48.8
C-14	84.5	85.1	85.7	84.4	[84.6]	84.8
C-15	32.1	32.3	32.6	32.2	[32.0]	32.3
C-16	26.6	26.9	26.9	27.0	[27.5]	27.1
C-17	55.1	54.4	54.8	53.9	[54.1]	53.9
C-18	15.8	15.9	15.9	15.9	[15.7]	16.1
C-19	23.8	23.7	23.7	23.9	[23.6]	23.8
C-20	162.7	155.5	156.3	155.6	[147.6]	150.9
C-22 [d]	96.7	129.3	124.8	119.5	[127.3]	121.8
C-23 [d]	118.1	198.8	191.7	167.9	[173.5]	168.5
$COCH_3$		26.4				
Ph 1			138.0			
Ph 2,6,3,5			128.4			
Ph 4			132.3			

[a] In p.p.m. downfield from $SiMe_4$ in $CDCl_3$–CD_3SOCD_3, δ($CDCl_3$) 78.8 unless otherwise stated. [b] In $CDCl_3$, δ 77.1. [c] In CD_3OD–$CDCl_3$–CD_3SOCD_3, δ($CDCl_3$) 78.8. [d] For numbering see structures (6)—(13).

TABLE 4

^{13}C Chemical shifts of L-rhamnopyranosides [a]

	α-L-Rhamnosides			α-L-Rhamnoside triacetates				Methyl β-L-rhamnoside triacetate
	(14)	(16)	(17)	(18) [b]	(18) [c]	(19) [d]	(15)	
C-1′	101.1	98.1	97.9	95.8	(95.5)	[95.2]	98.1	98.7
C-2′	70.4 *	71.1	70.9	70.6 *	(70.2) *	[70.1] *	69.3 *	86.6
C-3′	70.9 *	71.1	70.9	69.4	(69.3)	[69.2]	69.0 *	70.7
C-4′	72.2	72.3	72.3	71.3 *	(70.8) *	[70.7] *	70.4	70.5
C-5′	68.1	68.5	68.2	66.6	(66.3)	[66.2]	66.0	69.6
C-6′	17.8	17.8	17.7	17.5	(16.3)	[17.1]	17.3	17.3
C-1		30.3	*ca.* 37.0 [e]	30.4	(30.0)	[37.0]		
C-2		26.3 *	29.0	26.5	(25.9)	[28.6] **		
C-3		71.1	74.9	73.0	(73.1)	[76.6]		
C-4		29.4	33.8	29.7	(29.2)	[33.7]		
C-5		36.4	43.8	36.4	(36.5)	[44.1]		
C-6		26.5 *	28.5	26.5	(26.5) **	[28.5] **		
C-7		21.1	27.3	21.2	(20.9)	[27.3]		
C-8		41.0	40.8	41.9	(41.2)	[41.0]		
C-9		35.1	49.3	35.8	(35.3)	[49.6]		
C-10		34.9	35.5	35.3	(34.8)	[35.6]		
C-11		20.9	20.8	20.8	(20.9)	[21.0]		
C-12		39.3	39.1	40.1	(39.4)	[39.4]		
C-13		49.5	49.3	49.7	*e*	[49.6]		
C-14		83.9	83.7	85.5	(84.8)	[84.3]		
C-15		32.3	32.3	33.2	(31.9)	[32.3]		
C-16		26.5 *	26.5	26.9	(26.3) **	[26.7]		
C-17		50.5	50.5	51.0	*e*	[50.7]		
C-18		15.7	15.7	15.8	(14.9)	[15.6]		
C-19		23.7	12.0	23.8	(22.8)	[11.9]		
C-20		175.9	175.7	174.5	(176.8)	[176.0]		
C-21		73.1	73.1	73.4	(73.8)	[73.5]		
C-22		116.5	116.5	117.7	(116.3)	[116.8]		
C-23		173.5	173.8	174.5	*e*	[174.7]		
OMe	54.1						54.8	56.5
				20.8	(19.2)	[20.4]	20.5	20.4
OCO*Me*				21.3	(19.2)	[20.4]	20.5	20.6
				21.4	(19.2)	[21.0]	20.5	20.6
				169.9	(170.1)	[169.8]	169.6	169.4
O*C*OMe				169.9	(170.1)	[169.8]	169.6	169.4
				170.2	(170.1)	[170.3]	169.6	169.8

[a] In p.p.m. downfield from $SiMe_4$ in $CDCl_3$–CD_3SOCD_3 with δ($CDCl_3$) 78.8 unless otherwise stated. [b] In $CDCl_3$ solution, δ 77.1. [c] In CD_3OD solution, δ 47.5. [d] In $CDCl_3$–CD_3SOCD_3–CD_3OD, δ($CDCl_3$) 78.8. [e] Masked by solvent signals, or too weak.

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

TABLE 5

^{13}C Chemical shifts of D-glucopyranosides and D-galactopyranosides [a]

	β-D-Galactosides		β-D-Glucosides		β-D-Glucoside tetra-acetates			α-D-Glucoside tetra-acetates	
	(25) [b]	(26)	(20) [c]	(23)	(24)	(21) [d]	(22) [e]	[(21), α-1′-OMe] [d]	[(22), α-1′-OAc]
C-1′	{103.9}	101.9	{104.6}	101.2	97.7	100.7	91.3	96.7	89.0
C-2′	{70.8}	71.0	{74.6}	73.5	71.3 *	71.0	70.7	70.6	69.5
C-3′	{72.9}	73.8 *	{77.4}	77.0 *	72.3	72.5	72.5 *	70.0	70.0
C-4′	{68.8}	68.2	{71.2}	70.3	68.5	68.4	67.7	68.6	68.1
C-5′	{75.2}	74.9	{77.3}	76.4 *	70.9 *	71.0	72.7 *	67.2	70.0
C-6′	{61.1}	60.5	{62.4}	61.4	61.9	61.8	61.4	62.1	61.8
C-1		29.9		29.9	29.9				
C-2		26.2		26.4	26.1				
C-3		73.2 *		73.0	73.4				
C-4		29.7		29.5	29.2				
C-5		35.8		35.7	36.3				
C-6		26.6		26.6	26.6				
C-7		21.2		21.1	21.1				
C-8		41.1		41.0	41.1				
C-9		35.2		35.2	35.2				
C-10		34.9		34.9	34.9				
C-11		21.0		20.9	21.0				
C-12		39.5		39.5	39.3				
C-13		49.6		49.5	49.6				
C-14		84.0		84.0	84.0				
C-15		32.4		32.4	32.4				
C-16		26.6		26.6	26.6				
C-17		50.6		50.6	50.6				
C-18		15.7		15.7	15.7				
C-19		23.5		23.5	23.7				
C-20		176.0		175.8	175.9				
C-21		73.2		73.1	73.2				
C-22		116.6		116.6	116.6				
C-23		174.0		173.9	174.0				
OCH_3	{57.3}		{58.5}			56.5		55.4	
OCO*Me*					20.4 (4C)	20.4	20.9 (5C)	20.6 (4C)	20.8 (5C)
OCOMe					168.6	169.0	168.9	169.7	169.0
					169.1	169.2	169.4	170.1	169.4
					169.5	169.6	169.6	170.1	169.8
					170.0	170.0	169.9	170.5	170.0
							170.5		170.3

[a] In p.p.m. from $SiMe_4$ in $CDCl_3$–CD_3SOCD_3, δ($CDCl_3$) 78.8 unless otherwise stated. [b] Published data for D_2O solution (ref. 12). [c] Published data for D_2O solution (T. E. Walker, R. E. London, T. W. Whaley, R. Barker, and N. A. Matwiyoff, *J. Am. Chem. Soc.*, 1976, **98**, 5807). For data in pentadeuteriopyridine see ref. 17. [d] For assignments in $CDCl_3$, see ref. 13, and D. Y. Gagnaire, F. R. Taravel, and M. R. Vignon, *Carbohydr. Res.*, 1976, **51**, 157. [e] For assignments in $CDCl_3$, see H. Komura, A. Matsuno, Y. Ishido, K. Kushida, and K. Aoki, *Carbohydr. Res.*, 1978, **65**, 271.

* Signals within a vertical column may be interchanged.

5β-genins (see Tables 2 and 3). The 1.5 p.p.m. shielding of C-2 upon glycosidation at C-3 is characteristic of β-D- and α-L-pyranosides, and will be referred to later.

C-3 resonates in the same region as the oxygen-bearing carbons in the carbohydrate moiety, and signals for these carbons will be discussed in the section immediately following.

Carbohydrate Signals of Glycosides.—The carbon shieldings of methyl α-L-rhamnopyranoside (14) and of methyl α- and β-L-rhamnopyranoside triacetates were recorded in $CDCl_3$–CD_3SOCD_3 (Table 4) for comparison with those of the cardenolide L-rhamnosides in Table 4. Assignment of methyl α-L-rhamnoside (14) in $CDCl_3$–CD_3SOCD_3 follows from those of Kasai *et al.*,[10] Dorman and Roberts,[11] and Voelter *et al.*[12] for solutions in pentadeuteriopyridine, carbon disulphide, and deuterium oxide, respectively.

In the case of the methyl α- and β-L-rhamnopyranoside triacetates, Kalinovskii and Evtushenko [13] and Pozagay and Neszmély [14] gave assignments (for deuteriochloroform solutions) which were at variance with one another. Our assessment of the assignment starts from the expectation that C-4′ will be shielded to the same extent in both anomers (δ 70.4 and 70.5) and that C-3′ and C-5′ will be more shielded in the α-anomer which has an axial methoxy-group γ-gauche to these carbons. Comparing the α- and β-anomers, the shift difference at C-3′ (δ 69.0/69.3 *vs.* 70.7) is smaller than that at C-5′ (δ 66.0 *vs.* 69.6); C-3′ in the β-anomer is also shielded by the equatorial 1′-methoxy-group (periplanar heteroatom effect).[15] For each anomer, the highest-field methine carbon signal in the range δ 66—71 (α-anomer, δ 66.0; β-anomer, δ 69.6) has, in the s.f.o.r.d. spectrum, a smaller residual C–H coupling, compared to other signals in the region, when the proton-decoupling frequency is placed at the high-field end of the ^1H resonance frequency range. This implies that this methine carbon has a relatively shielded attached proton. Evidence is thus available that these signals are those of C-5′; as carbons 2′, 3′, and 4′, but not 5′, are attached to electron-

withdrawing acetoxy-groups. Our assignments are in agreement with those of Kalinovskii and Evtushenko.[13]

Signals due to the carbohydrate carbons of digitoxigenin β-D-galactoside (26), β-D-glucoside (23), and β-D-glucoside tetra-acetate (24) listed in Table 5 are assigned by comparison with the data (also shown in Table 5) of the corresponding 1′-methyl and 1′-acetyl β-D-pyranosides. From considerations of internal consistency, C-3 of the steroid aglycone has been allocated a chemical shift of *ca.* δ 73 for these three digitoxigenin β-D-glycosides (Table 5), *ca.* δ 71 for digitoxigenin α-L-rhamnoside (16) (Table 4), and *ca.* δ 75 for uzarigenin α-L-rhamnoside (17) (Table 4), all shifts referring to $CDCl_3$–CD_3SOCD_3 solvent.

Glycosidation Shifts.—In a study of the conformational properties of glycosidic linkages, Lemieux and Kato [16] proposed, using n.m.r. results and hard-sphere calculations, that the *exo*-anomeric effect offers resistance to rotation about the anomeric-carbon to glycosidic-oxygen bond (ϕ angles) and that the preferred conformation for a glycopyranoside arises mainly from rotation about the aglycone-carbon to glycosidic-oxygen bond (ψ angles). In support, Tori, Tanaka, and their respective co-workers [17,10] showed that on glycosidation of a chiral and unhindered secondary alcohol, the two β-carbons on the alcohol are shielded to unequal extents. A β-D- or an α-L-glycoside group shields the pro-*S*-carbon (by *ca.* 4 p.p.m.) more than the pro-*R*-carbon (by *ca.* 2 p.p.m.), but an α-D- or a β-L-glycoside has less shielding on the pro-*S*-carbon (*ca.* 2 p.p.m.) compared to the pro-*R*-carbon (*ca.* 4 p.p.m.). Effects on the γ-carbons are <0.7 p.p.m. Shift changes upon glycosidation (glycosidation shifts) of digitoxigenin and uzarigenin as derived from the data in Tables 2 and 3 are shown in Table 6. These glycosidation shifts are analogous to those reported by the Japanese workers [10,17] for 3β-hydroxy-steroids (5β and 5α), and provides support for the configuration of the anomeric carbons in our semi-synthetic cardenolide glycosides.

It was noted by Kasai *et al.*[10] that for pyranosides of various alcohols, C-2′ and other carbohydrate carbons (other than the anomeric one) have ^{13}C shieldings which are essentially the same as those of the methyl glycoside of the same anomeric configuration. This observation, which is substantiated in the case of glucosides by the data of Tori and his co-workers,[17] probably has its origin in the high preference for C-2′ to be *anti* to the α-carbon of the alcohol.[16] Our data in Tables 4 and 5 do show parallel chemical shifts when methyl β-D-galactopyranoside (25), methyl β-D-glucopyranoside (20), and methyl β-D-glucopyranoside tetra-acetate (21) are compared with the appropriate digitoxigenin β-D-glycosides (Table 5), and when methyl α-L-rhamnopyranoside (14) is compared with the α-L-rhamnosides (16) and (17) of digitoxigenin and uzarigenin (Table 4). When instead the methyl α-D- or β-L-glycoside peracetates (see Tables 4 and 5) are used for comparison, chemical-shift differences are observed for C-5′ and (to a lesser extent) for C-2′, due to γ-gauche shielding of these carbons by the axial 1′-alkoxy-group in α-D- and β-L-glycosides.

TABLE 6

^{13}C Chemical shift changes (p.p.m.) upon glycosidation.[a] For aglycone carbons, δ(glycoside) − δ(aglycone); for carbohydrate carbons δ(glycoside) − δ(methylglycoside)

Carbon	C-3	C-2 (pro-*R*)	C-4 (pro-*S*)	C-1	C-5	C-1′
Relation to glycosidic O	α	β	β	γ	γ	
Digitoxigenin β-D-galactoside (26)	+8.2 to 8.8	−1.5	−3.5	+0.3	0	
Digitoxigenin β-D-glucoside (23)	+8.0	−1.3	−3.7	+0.3	−0.1	
Digitoxigenin β-D-glucoside tetra-acetate (24)	+8.4	−1.6	−4.0	+0.3	+0.5	−3.0
Digitoxigenin α-L-rhamnoside (16)	+6.1	−1.4	−3.8	+0.7	+0.8	−3.0
Digitoxigenin α-L-rhamnoside triacetate (18)	+6.3 [b]	−1.3 [b]	−3.4 [b]	+0.8 [b]	+0.5 [b]	(−2.3) [b]
Uzarigenin α-L-rhamnoside (17)	+5.2	−2.2	−4.2	*ca.* 0 [d]	−0.5	−3.2
Uzarigenin α-L-rhamnoside triacetate (19)	(+6.9) [c]	(−2.6) [c]	(−4.3) [c]	(0) [c]	(−0.2) [c]	(−2.9) [c]

[a] Shift changes refer to $CDCl_3$–CD_3SOCD_3 except those referred to in footnotes *b* and *c*. [b] Chemical shifts of the glycoside in $CDCl_3$ compared with chemical shifts of the genin also in $CDCl_3$ but of the methylglycoside in $CDCl_3$–CD_3SOCD_3 (Tables 1 and 4). [c] Chemical shifts of the glycoside in CD_3OD–CD_3SOCD_3–$CDCl_3$ mixture compared with the chemical shifts of the genin and of the methylglycoside in CD_3SOCD_3–$CDCl_3$ solutions (Tables 1 and 4). [d] Signal of C-1′ in glycoside masked by solvent peaks.

EXPERIMENTAL

^{13}C N.m.r. spectra were determined on a Varian CFT-20 spectrometer operating at 20 MHz in the Fourier-transform mode. Acquisition time of 0.45 s with no pulse delay, pulse width of 6 μs; *ca.* 0.5M solutions were used. Preparation of the compounds is described in refs. 1 and 8. Solvent $CDCl_3$–CD_3SOCD_3 (1 : 2).

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