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The Fucofuranoside Method, a New ^{1}H and ^{13}C Nuclear Magnetic Resonance Method to Determine the Absolute Configuration of Secondary Alcohols

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Abstract: A new ^{1}H and ^{13}C NMR method for determining the absolute configuration of secondary alcohols, using their β-D- and β-L-fucofuranosides, has been devised. The conformations of the two enantiomeric furanosyl groups are symmetrical in the symmetrically substituted furanosides (Fig. 3), whereas they are unsymmetrical in the unsymmetrically substituted furanosides (Fig. 7). The $\Delta\delta_H{}^p$ (^{1}H) and $\Delta\delta_C{}^p$ (^{13}C) values (Fig. 4 and 6) were obtained by subtracting the chemical shifts, in pyridine-d_5, of the β-D-isomer from the corresponding chemical shifts of the β-L-isomer. The ^{1}H NMR analysis utilizes the strong anisotropy of the solvent which, *solvated* to the fucofuranosyl group, exerts uneven influences on the aglycon. The $\Delta\delta_H{}^p$ values are positive for the protons of the right segment (R_r in Fig. 3), and negative for the protons of the left segment (R_l).

In the ^{13}C NMR, the two glycosides experience glycosidation shifts in the opposite way. In the symmetrically substituted furanosides, the $\Delta\delta_C{}^p$ values are positive for the right β-carbon and negative for the left β-carbon (Fig. 6, **1a**,**b** and **6a**,**b**). In the unsymmetrically substituted furanosides, the $\Delta\delta_C{}^p$ values of the anomeric, α- and the left β-carbons of the *(S)* -type β-fucofuranosides (**2a**,**b** and **3a**,**b**) are negative. In contrast, the $\Delta\delta_C{}^p$ values of the anomeric, α- and the right β-carbons of the *(R)* -type β-fucofuranosides (**4a**,**b** and **5a**,**b**) are positive. A similar $\Delta\delta_C{}^p$ pattern was shown to exist in the β-D- and β-L-glucopyranosides (Fig. 8), and even in the β-D- and α-D-glucopyranosides (Fig. 10). © 1997 Elsevier Science Ltd.

Introduction

In stereochemical studies of natural products, it is of fundamental importance to determine the absolute configuration of the secondary hydroxyl groups. For that purpose, convenient ^{1}H NMR procedures popularly employed at present are the MTPA (2-methoxy-2-trifluoromethylphenylacetic acid) and *O*-methylmandelate ester methods, both first introduced by Dale and Mosher.[1,2] Recently, other new chiral substituents have been proposed; e.g., the tetra-*O*-benzoylglucosyl group,[3] and several aryl methoxyacetic acids[4] which have more powerful anisotropic effects than the phenyl substituent of the above methods. All of these methods follow virtually the same principles, using the diamagnetic effects of the chiral ester substituents or tetra-*O*-benzoylglucopyranosyl group, which directly influence the protons of the alcohol moiety. To be applicable generally, however, they all have the same limitations: **1**) Their ^{13}C NMR spectra do not provide any information concerning the configuration[5]; **2**) If the conformations of the substituents are unfavorable, effective diamagnetic effects, to the protons, will not be available.

The MTPA method, for example, requires the major rotamer of both the *(R)*- and *(S)*-ester substituents to take the conformation in which the carbinyl proton, the ester carbonyl group and the trifluoromethyl group are nearly eclipsed. But, when the substituent is axially oriented, owing to its repulsion from the 1,3-synperiplanar substituents or protons, it often takes a sterically unfavorable conformation and thus the method is rendered inapplicable. The recently proposed more powerful but bulkier ester groups having a naphthyl or anthryl substituent,[4] and also the tetra-*O*-benzoylglucopyranosyl group,[3] must suffer more severe steric hindrances.

The present paper proposes a new method based on a different approach, using ^1H and ^{13}C NMR spectra simultaneously. This, the fucofuranoside method, has several advantageous characteristics: **1**) For the ^1H NMR analyses, it utilizes not the direct anisotropy of the substituent, but the strong anisotropy of pyridine, the solvent which *solvates* to the polar substituent; **2**) As polar and chiral substituents, the β-D- and β-L-fucofuranosyl groups are used for their orientation effect (exo-anomeric effect)[6] on the aglycon; **3**) Its conformation is therefore more rigid than that of the ester linkages so that it is applicable to axial hydroxyl groups; **4**) The specific non-bonded interactions due to the glycosidic linkages cause carbon chemical shifts remarkably different between the two diastereomeric glycosides; **5**) Most important, because of this last fact, the ^{13}C NMR can be used, for the first time, as a reliable tool to determine the configurations.

^1H NMR Spectra for Determination of Absolute Configuration

Symbols used for the ^1H NMR chemical shifts of β-D- and β-L-fucofuranosides

In the ^1H NMR analyses, the present method utilizes simply the difference in the chemical shifts ($\Delta\delta_H^P$) between β-D- and β-L-fucofuranoside in pyridine-d_5 ($\delta_{C_5D_5N}^L - \delta_{C_5D_5N}^D$, Table 1). In order to estimate the pyridine-induced contributions (p-shifts), the chemical shifts in $CDCl_3$ were measured simultaneously. The $\Delta\delta_H^c$ value indicates the difference in the chemical shifts between the two diastereomers in $CDCl_3$ ($\delta_{CDCl_3}^L - \delta_{CDCl_3}^D$). The p-shifts in the β-D- and β-L-isomers were defined as $\Delta\delta_H^D$ and $\Delta\delta_H^L$, respectively. The $\Delta\Delta\delta_H$ value indicates the difference in the p-shift values between the two diastereomers ($\Delta\delta_H^L - \Delta\delta_H^D$). The relations between these symbols are: $\Delta\Delta\delta_H = (\delta_{C_5D_5N}^L - \delta_{CDCl_3}^L) - (\delta_{C_5D_5N}^D - \delta_{CDCl_3}^D) = (\delta_{C_5D_5N}^L - \delta_{C_5D_5N}^D) - (\delta_{CDCl_3}^L - \delta_{CDCl_3}^D) = \Delta\delta_H^P - \Delta\delta_H^c$

For example, the chemical shifts (Experimental) of the 2α-H of cholesterol β-fucofuranosides are 2.17 ppm ($\delta_{C_5D_5N}^D$) and 1.84 ppm ($\delta_{CDCl_3}^D$) in the β-D-isomer (**1a**), whereas they are 2.00 ppm ($\delta_{C_5D_5N}^L$) and 1.92 ppm ($\delta_{CDCl_3}^L$) in the β-L-isomer (**1b**). From these four values, the differences between the two diastereomers ($\Delta\delta_H^P$ -0.17 ppm and $\Delta\delta_H^c$ + 0.08 ppm), the p-shifts $\Delta\delta_H^D$ (+0.33 ppm) and $\Delta\delta_H^L$ (+0.08 ppm), and their difference $\Delta\Delta\delta_H$ (-0.25 ppm) were derived (Table 1). The negative $\Delta\delta_H^D$ and $\Delta\delta_H^L$ values (e.g., 1α-H of **1a**,**b**) show that the chemical shift is more upfield-shifted in pyridine-d_5 than in $CDCl_3$.

Pyridine-induced anisotropic effects

The pyridine-induced anisotropic effect (p-shift) is practically equivalent to the difference in the ^1H NMR chemical shifts in pyridine-d_5 (p) relative to $CDCl_3$ (c). A typical example is the deshielding effect for the protons and methyl groups having 1,3-synperiplanar or geminal, or gauche relations with respect to the polar hydroxyl function. Their magnitudes, observed for steroids and other classes of compounds having a single hydroxyl group, are generally less than + 0.3 ppm.[7] However, we noticed that remarkably large paramagnetic shifts occur when protons were influenced doubly by such hydroxyl groups. The p-shifts for the protons observed in 1β,3β,5α,6β-tetrahydroxysteroids isolated from soft corals, for example, amounted to + 0.79 to + 0.93 ppm.[8] It was expected that the uneven secondary magnetic field of the pyridine molecules, associated to the polar sites of a chiral substituent, may cause an uneven paramagnetic effect on the nearby protons. *If the two polar and enantiomeric substituents exert the influences of different magnitudes, then such differences can be used for predicting the absolute configuration of the hydroxyl group.*

Pyridine-induced shifts in α-L-fucopyranoside and β-D- and β-L-fucopyranosides

Previously we isolated several 3β-hydroxy Δ^5-steroid-type 3-*O*-α-L-fucopyranosides from soft corals.[9] Their ^{1}H NMR spectra indicated that the allylic protons at C-4 were influenced by significant p-shifts (4α-H, + 0.29 ppm; 4β-H, + 0.23 ppm, Fig. 1, **A**). Such deshieldings can only be rationalized as due to the influence of the 2'-OH of the α-L-fucopyranosyl group. Fucose is commercially available in both D- and L-forms, and shows good solubility of 6-deoxysugars. The spatial arrangement of the 2'-OH, with respect to the 4-H_2 of the steroidal aglycon in the α-L-fucopyranoside, was assumed to be similar to that in the β-D-fucopyranoside (**B**). The β-anomers are, usually, the easier derivatives because of the neighboring effect of the 2'α-OH.[7] For the model compounds, the β-D- and β-L-fucopyranosides (**B** and **C**) of cholesterol (**1**) were synthesized.[10e] However, the ^{1}H NMR experiment revealed that both the β-D- and β-L-isomers show substantial p-shifts at 4-H_2 in almost the same magnitude. Apparently, in such β-fucopyranosides, the p-shifts occur not only due to the 2'-OH of the pyranose (oxy-side), but also due to the ring-oxygen atom side (oxa-side) where the dipole involving *O*-5' attracts pyridine molecules.

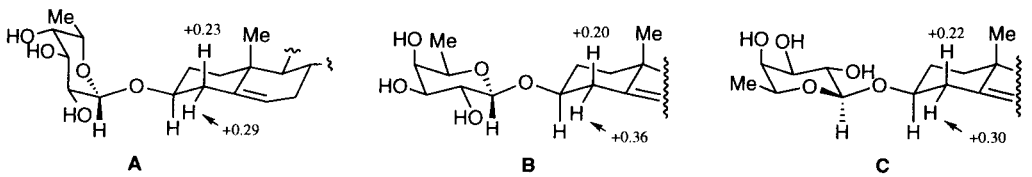


Fig. 1 Pyridine-induced shifts (in ppm) in ergost-5-en-3β-ol 3-*O*-α-L-fucopyranoside (**A**), cholest-5-en-3β-ol 3-*O*-β-D-fucopyranoside (**B**) and cholest-5-en-3β-ol 3-*O*-β-L-fucopyranoside (**C**).

Pyridine-induced shifts in β-D- and β-L-fucofuranosides

Subsequently, cholesterol was converted to β-D- and β-L-fucofuranosides (**1a**,**b**) (Fig. 2, Table 1). The enantiomeric β-fucofuranosyl groups were found to cause remarkably different influences. The β-D-isomer (**1a**) showed larger p-shifts ($\Delta\delta_H^D$) for 2-H_2 (2α-H, + 0.33 ppm; 2β-H, + 0.19 ppm) than the p-shifts ($\Delta\delta_H^L$) in the β-L-isomer (**1b**) (2α-H, + 0.08 ppm; 2β-H, + 0.15 ppm). In contrast, the β-L-isomer (**1b**) showed larger p-shifts for 4-H_2 (4α-H, + 0.43 ppm; 4β-H, + 0.28 ppm) than the β-D-isomer (**1a**) (4α-H, + 0.18 ppm; 4β-H, +0.21 ppm). Apparently, in the two β-fucofuranosides, the p-shifts due to their oxa-side are substantially larger than the p-shifts due to their oxy-side. The $\Delta\Delta\delta_H$ values ($\Delta\delta_H^L - \Delta\delta_H^D$) derived for 2-$H_2$ and 4-H_2 are nearly equivalent in size but opposite in sign (e.g., - 0.25 ppm for 2α-H and + 0.25 ppm for 4α-H).

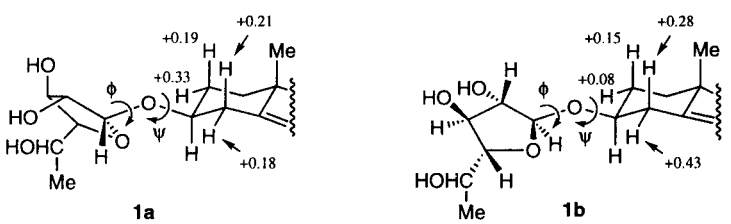


Fig. 2 Pyridine-induced shifts (in ppm) in cholest-5-en-3β-ol 3-*O*-β-D-fucofuranoside (**1a**) and cholest-5-en-3β-ol 3-*O*-β-L-fucofuranoside (**1b**).

Lemieux and Koto have estimated the torsion angles of the anomeric proton to carbinyl carbon (ϕ angle, + 55°), and of the anomeric carbon to carbinyl proton (ψ angle, + 10°) of cyclohexyl β-D-glucopyranoside based upon the hard-sphere calculation and molecular rotation.[11] The conformation of the β-D-monofucofuranosidic linkage is unknown, but its ϕ and ψ angles should not be very different from these values. The above results are consistent with this conformation, since when it was applied to the β-D-fucofuranoside (**1a**) and to the β-L-fucofuranoside (**1b**, ϕ = - 55°, ψ = - 10°) (Fig. 2 and 3), the carbinyl proton (3α-H) should be positioned at nearly equal distances with regard to the anomeric proton and to the 4'-*O* atom; the C-2' in the sugar moiety and the C-3 carbinyl carbon are nearly antiperiplanar to each other. Nuclear Overhauser enhancement (NOE) was observed for 3α- and 4α-H, by irradiation of 1'-H, both in the β-D-fucopyranoside (Fig. 1, **B**, 3α-H, 6.6 %; 4α-H, 2.8%) and in the β-D-fucofuranoside (Fig. 2, **1a**, 3α-H, 5.6 %; 4α-H, 1.6 %), supporting their common conformation. Apparently, in such conformation, the oxy- and oxa-sides of the β-fucopyranosyl groups, and the oxa-side of the β-fucofuranosyl groups, are juxtaposed to the β-positions of the aglycon close enough to cause substantial p-shifts (Fig 1, 2 and 3). In contrast, the 2'-OH of the β-fucofuranosyl groups remains at a remote site, so that their oxy-side has less influence on the aglycon.

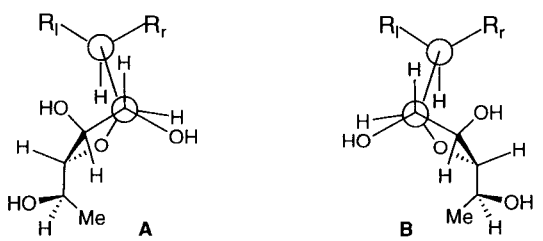


Fig. 3 Front view of the presumed conformation of the glycosidic linkages of β-D-fucofuranoside (**A**) and β-L-fucofuranoside (**B**).

The $\Delta\delta_H{}^p$ values

The $\Delta\delta_H{}^p$ values are more convenient than the $\Delta\Delta\delta_H$ values, since they are available from only two spectra in pyridine-d_5 , and show rather better correlations (Table 1) in the reference compounds **1** to **7**. This is because the magnitudes of $\Delta\delta_H{}^c$ values are sufficiently small. They either contribute to the $\Delta\delta_H{}^p$ ($\Delta\Delta\delta_H$ + $\Delta\delta_H{}^c$) values, or they are cancelled out by the larger $\Delta\Delta\delta_H$ when the signs of $\Delta\Delta\delta_H$ and $\Delta\delta_H{}^c$ were opposite. It was concluded, therefore, that for the application of the present method, the spectra taken in $CDCl_3$ are unnecessary. Also, in the unsymmetrically substituted glycosides, both the $\Delta\delta_H{}^p$ and $\Delta\delta_H{}^c$ values of the carbinyl (α-) proton predict the configuration (see below). Since their magnitudes are comparable, they almost cancel out each other in the $\Delta\Delta\delta_H$ value ($\Delta\delta_H{}^p$ - $\Delta\delta_H{}^c$).

General procedure

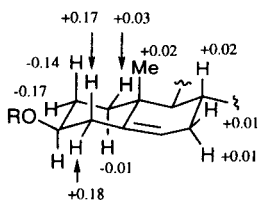
Secondary alcohols were treated in CH_2Cl_2 with fucofuranose tetraacetate, TMSOTf and 4A molecular sieve (r.t., ca. 30 min).[10e] The unstable compounds in this condition can be glycosidated using the corresponding 1'-bromosugar and silver zeolite.[12] Alkaline hydrolysis followed by column chromatography gives the β-fucofuranosides in high yields. The NMR (^1H and ^{13}C) spectra of the two diastereomeric glycosides were measured at identical concentration and temperature. When the two glycosides are viewed as illustrated in Fig.

3, placing the furanosyl group in front and the carbinyl proton down, the $\Delta\delta_H{}^P$ values should be negative for the protons in the left segment (R_l) and positive for the protons in the right segment (R_r), in the conventional way as practiced in the MTPA determination.[1]

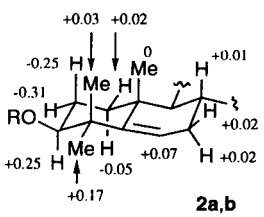
Application

The $\Delta\delta_H{}^P$ values were derived for seven typical known chiral alcohols, which are symmetrical (**1**, **6**, **7**) or unsymmetrical (**2**-**5**) at β-positions, and cyclic (**1**-**6**) or acyclic (**7**) (Fig. 4 and Table 1, last column). In compound **6**, the hydroxyl group is axially-oriented. Other four $\Delta\delta_H$ values ($\Delta\delta_H{}^D$, $\Delta\delta_H{}^L$, $\Delta\delta_H{}^c$ and $\Delta\Delta\delta_H$) are also given in Table 1, for comparison with $\Delta\delta_H{}^P$ values. The chemical shifts were assigned from the characteristic coupling patterns, H-H COSY and HSQC spectra, and confirmed by NOE differential spectra.

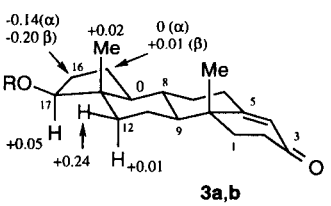
All of these β-fucofuranosides show substantial $\Delta\delta_H{}^P$ values for the protons or substituents at β-positions. Practically, the $\Delta\delta_H{}^P$ values up to a magnitude of 0.02 ppm should rather be regarded as less meaningful. In the β-fucofuranosides of cholesterol (**1a,b**), nearly equivalent magnitudes of negative and positive $\Delta\delta_H{}^P$ values were derived for the 2-H_2 and 4-H_2. The β-fucofuranosides of 4,4-dimethylcholesterol (**2a,b**) bear bulky substituents at C-4, but the distinct negative and positive $\Delta\delta_H{}^P$ values for 2-H_2 and 4,4-dimethyl group are retained. The 1β-H showed opposite but numerically less significant values in **1a,b** and **2a,b**. The same pattern was observed for 16-H_2, 12-H_2 and 18-H_3 of testosterone β-fucofuranosides (**3a,b**).



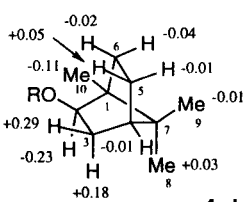
1a,b



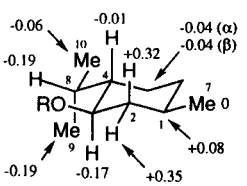
2a,b



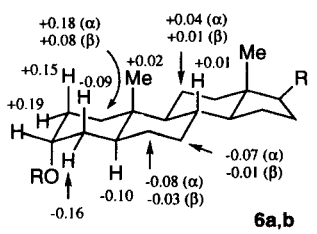
3a,b



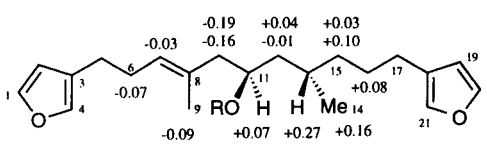
4a,b



5a,b



6a,b



7a,b

Fig. 4 The $\Delta\delta_H{}^P$ values observed for the protons of the β-D- and β-L-fucofuranoside derivatives of the chiral secondary alcohols **1** to **7** (400 MHz, in ppm).

The $\Delta\delta_H{}^p$ values due to 6-H_2 and 10-H_3 of the β-fucofuranosides of (1*S*)-*endo*-(-)-borneol (**4a,b**) are negative, whereas those due to 3-H_2 are positive. Exactly negative and positive $\Delta\delta_H{}^p$ values are derived for the left and the right segment protons, respectively, of the β-fucofuranosides of (-)-menthol (**5a,b**). For comparison, the $\Delta\delta_H$ values for (-)-menthol (**5**), previously derived by the MTPA[1f] and tetra-O-benzoylglucoside methods,[3] are shown in Fig. 5.

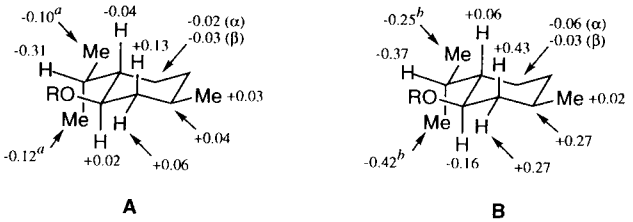


Fig. 5 The $\Delta\delta_H$ values (in ppm) reported for the MTPA (**A**, $\delta_H{}^S - \delta_H{}^R$) and tetra-*O*-benzoyl-β-glucopyranoside (**B**, $\delta_H{}^L - \delta_H{}^D$) derivatives of (-)-menthol (**5**). ^{a,b}Assignments interchangeable.

Previously proposed chiral ester groups as NMR indicators have a common shortcoming in that their conformations are rather unstable; if their diamagnetic substituents diverge from the pertinent direction, meaningful $\Delta\delta_H$ values will not be available. Axially-oriented MTPA ester groups often take sterically unfavorable conformations; usually it is not possible to recognize their actual conformations in solution. One of the advantages of the present method is that glycosidic linkages generally have an orientation effect (exo-anomeric effect)[6] on the aglycon so that they are more resistant to rotation. Unsuitable conformations could be recognized by the weakness or absence of the NOE between the carbinyl and the anomeric protons. When the fucofuranoside method was applied to the axial hydroxyl group of 5α-cholestane-3α-ol (**6**), it showed quite definite $\Delta\delta_H{}^p$ values, even for the remote α-side protons such as 6α-H and 7α-H (Fig. 4). The NOEs between 1'-H and 3β-H observed in the β-D- (**6a**, 7.3%) and in the β-L-isomer (**6b**, 8.3%) show that the pertinent conformations were retained in such axially-oriented furanosyl groups as well. Consequently, the furanosyl substituents are located closer to the α-side protons of the aglycon and deshield them strongly.

(+)-Furospongin-1 (**7**) is a typical C_{21} furanoterpene, isolated from the sponges *Spongia officinalis* and *Hippospongia communis* in 1971.[13] The absolute configuration at C-11 had been derived as (11*S*) by using the Horeau determination.[14] Application of the Horeau method is, however, inappropriate since the asymmetric carbinyl carbon is linked to two sterically equivalent methylene groups. Recently we isolated (+)-furospongin-1 from the sponge *Phyllospongia foliascens* and proved the absolute configuration as (11*R*) based on four factors (coupling pattern of 12-H_2, p-shifts, NOEs and MTPA determination).[15] Application of the fucofuranoside method to **7** gave straightforward results; the $\Delta\delta_H{}^p$ values are distributed in an orderly way, negative for the protons in the left segment, and positive for those in the right segment, confirming the revised structure. In the β-fucofuranosides of the cyclic alcohols **1a,b** to **6a,b**, the significant $\Delta\delta_H{}^p$ values are available mainly for the β-protons or β-substituents, though theoretically it is sufficient for the judgement of configuration. However, in a linear structure such as **7a,b**, the paramagnetic effect of the associated pyridine molecules are elongated to fairly remote protons such as 6-H_2 and 16-H_2.

Table 1 $\Delta\delta_H$ Values (in ppm) derived from the ^1H NMR chemical shifts of the β-D- and β-L-fucofuranosides of the chiral secondary alcohols **1** to **7** in $CDCl_3$[a] and in pyridine-d_5[a] ($\Delta\delta_H{}^P = \Delta\Delta\delta_H + \Delta\delta_H{}^C$).

Cholesterol β-fucofuranosides (**1a,b**)						4,4-Dimethylcholesterol β-fucofuranosides (**2a,b**)					
Proton[b]	$\Delta\delta_H{}^D$[c]	$\Delta\delta_H{}^L$[d]	$\Delta\Delta\delta_H$[e]	$\Delta\delta_H{}^C$[f]	$\Delta\delta_H{}^P$[g]	Proton	$\Delta\delta_H{}^D$	$\Delta\delta_H{}^L$	$\Delta\Delta\delta_H$	$\Delta\delta_H{}^C$	$\Delta\delta_H{}^P$
1α (l)	-0.08	-0.05	+0.03	-0.04	-0.01	1α (l)	-0.07	-0.08	-0.01	-0.04	-0.05
1β (l)	-0.09	-0.09	0	+0.03	+0.03	1β (l)	-0.07	-0.10	-0.03	+0.05	+0.02
2α (l)	+0.33	+0.08	-0.25	+0.08	-0.17	2α (l)	+0.34	+0.10	-0.24	-0.07	-0.31
2β (l)	+0.19	+0.15	-0.04	-0.10	-0.14	2β (l)	+0.22	+0.06	-0.16	-0.09	-0.25
11α (l)	-0.03	-0.02	+0.01	0	+0.01	11α (l)	-0.01	-0.01	0	0	0
11β (l)	-0.03	-0.02	+0.01	0	+0.01	11β (l)	-0.01	-0.01	0	0	0
3α	+0.22	+0.22	0	0	0	3α	+0.15	+0.23	+0.08	+0.17	+0.25
4α (r)	+0.18	+0.43	+0.25	-0.07	+0.18	4α-Me (r)	+0.17	+0.32	+0.15	+0.02	+0.17
4β (r)	+0.21	+0.28	+0.07	+0.10	+0.17	4β-Me (r)	+0.24	+0.25	+0.01	+0.02	+0.03
6 (r)	-0.03	-0.03	0	0	0	6 (r)	+0.04	+0.08	+0.04	+0.03	+0.07
7α (r)	+0.03	+0.02	-0.01	+0.02	+0.01	7α (r)	+0.05	+0.07	+0.02	0	+0.02
7β (r)	-0.06	-0.05	+0.01	0	+0.01	7β (r)	-0.01	+0.01	+0.02	0	+0.02
8 (r)	-0.05	-0.03	+0.02	0	+0.02	8 (r)	-0.01	0	+0.01	0	+0.01
9	-0.02	0	+0.02	+0.01	+0.03	9	0	+0.01	+0.01	-0.01	0
18	0	0	0	+0.01	+0.01	18	+0.02	+0.02	0	+0.01	+0.01
19	-0.03	-0.01	+0.02	0	+0.02	19	+0.06	+0.04	-0.02	+0.02	0
1'	+0.50	+0.47	-0.03	0	-0.03	1'	+0.45	+0.44	-0.01	+0.09	+0.08
6'	+0.31	+0.29	-0.02	+0.01	-0.01	6'	+0.30	+0.28	-0.02	0	-0.02

Testosterone β-fucofuranosides (**3a,b**)						[(1S)-endo]-(-)-Borneol β-fucofuranosides (**4a,b**)					
Proton	$\Delta\delta_H{}^D$	$\Delta\delta_H{}^L$	$\Delta\Delta\delta_H$	$\Delta\delta_H{}^C$	$\Delta\delta_H{}^P$	Proton	$\Delta\delta_H{}^D$	$\Delta\delta_H{}^L$	$\Delta\Delta\delta_H$	$\Delta\delta_H{}^C$	$\Delta\delta_H{}^P$
15α (l)	-0.16	-0.19	-0.03	+0.03	0	6-*exo* (l)	0	-0.05	-0.05	+0.01	-0.04
15β (l)	-0.10	-0.12	-0.02	+0.03	+0.01	6-*endo* (l)	+0.48	+0.47	-0.01	-0.01	-0.02
16α (l)	+0.07	-0.06	-0.13	-0.01	-0.14	8 (l)	-0.11	-0.08	+0.03	0	+0.03
16β (l)	+0.29	+0.10	-0.19	-0.01	-0.20	9 (l)	-0.06	-0.07	-0.01	0	-0.01
17	+0.14	+0.09	-0.05	+0.10	+0.05	10 (l)	+0.15	+0.03	-0.12	+0.01	-0.11
7α (r)	-0.19	-0.18	+0.01	0	+0.01	2	+0.17	+0.16	-0.01	-0.22	-0.23
7β (r)	-0.22	-0.21	+0.01	-0.01	0	3-*exo* (r)	-0.04	+0.03	+0.07	+0.11	+0.18
8 (r)	-0.18	-0.18	0	+0.02	+0.02	3-*endo* (r)	+0.10	+0.40	+0.30	-0.01	+0.29
9 (r)	-0.20	-0.19	+0.01	0	+0.01	4 (r)	-0.12	-0.08	+0.04	-0.05	-0.01
11α (r)	-0.23	-0.21	+0.02	0	+0.02	5-*exo* (r)	-0.05	-0.05	0	-0.01	-0.01
11β (r)	-0.16	-0.12	+0.04	-0.02	+0.02	5-*endo* (r)	0	+0.10	+0.10	-0.05	+0.05
12α (r)	-0.11	-0.08	+0.03	-0.02	+0.01	1'	+0.41	+0.44	+0.03	-0.01	+0.02
12β (r)	+0.02	+0.31	+0.29	-0.05	+0.24	6'	+0.26	+0.26	0	0	0
14 (r)	-0.19	-0.21	-0.02	+0.02	0						
18 (r)	+0.11	+0.14	+0.03	-0.01	+0.02						
19 (r)	-0.18	-0.17	+0.01	0	+0.01						
1'	+0.46	+0.43	-0.03	-0.05	-0.08						
6'	+0.30	+0.32	+0.02	0	+0.02						

The $\Delta\delta_H{}^P$ and $\Delta\delta_H{}^C$ values at carbinyl protons

The unsymmetrically substituted compounds **2a,b** to **5a,b** show substantially large positive or negative $\Delta\delta_H{}^P$ (and $\Delta\delta_H{}^C$, Table 1) values for the carbinyl protons (Fig. 4). The same phenomenon has previously been referred to for the tetra-*O*-benzoylglucopyranosides (in $CDCl_3$)[3] without explanation so that it is worthy of comment. In compounds **2a,b** and **3a,b**, the sequence of the furanosyl group, the sterically larger and then smaller of the two substituents, is counterclockwise (*S*-type). Their $\Delta\delta_H{}^P$ and $\Delta\delta_H{}^C$ values of the carbinyl proton are positive. In contrast, these values are negative if the sequence is clockwise (*R*-type) as observed in

Table 1.(*contd*)

(-)-Menthol β-fucofuranosides (**5a,b**)

Proton	$\Delta\delta_H{}^D$	$\Delta\delta_H{}^L$	$\Delta\Delta\delta_H$	$\Delta\delta_H{}^c$	$\Delta\delta_H{}^p$
4 (l)	+0.10	+0.14	+0.04	-0.05	-0.01
5α (l)	-0.05	-0.08	-0.03	-0.01	-0.04
5β (l)	-0.09	-0.10	-0.01	-0.03	-0.04
8 (l)	+0.58	+0.32	-0.26	+0.07	-0.19
9 (l)	+0.16	-0.02	-0.18	-0.01	-0.19
10 (l)	-0.04	-0.07	-0.03	-0.03	-0.06
3	+0.13	+0.10	-0.03	-0.14	-0.17
1 (r)	-0.19	-0.16	+0.03	+0.05	+0.08
2α (r)	+0.03	+0.36	+0.33	+0.02	+0.35
2β (r)	-0.01	+0.22	+0.23	+0.09	+0.32
7 (r)	-0.09	-0.09	0	0	0
6α	-0.11	-0.11	0	-0.02	-0.02
6β	-0.12	-0.06	+0.06	-0.06	0
1'	+0.41	+0.44	+0.03	-0.08	-0.05
6'	+0.29	+0.26	-0.03	+0.02	-0.01

5α-Cholestan-3α-ol β-fucofuranosides (**6a,b**)

Proton	$\Delta\delta_H{}^D$	$\Delta\delta_H{}^L$	$\Delta\Delta\delta_H$	$\Delta\delta_H{}^c$	$\Delta\delta_H{}^p$
1α (r)	+0.23	+0.40	+0.17	+0.01	+0.18
1β (r)	-0.07	-0.01	+0.06	+0.02	+0.08
2α (r)	+0.11	+0.40	+0.29	-0.10	+0.19
2β (r)	-0.05	-0.03	+0.02	+0.13	+0.15
11α (r)	-0.02	+0.03	+0.05	-0.01	+0.04
11β (r)	0	+0.01	+0.01	0	+0.01
3	+0.13	+0.14	+0.01	-0.01	0
4α (l)	+0.34	+0.17	-0.17	+0.01	-0.16
4β (l)	-0.01	+0.01	+0.02	-0.11	-0.09
5 (l)	+0.43	+0.35	-0.08	-0.02	-0.10
6α (l)	+0.06	-0.03	-0.09	+0.01	-0.08
6β (l)	+0.01	-0.03	-0.04	+0.01	-0.03
7α (l)	+0.01	-0.07	-0.08	+0.01	-0.07
7β (l)	-0.02	-0.03	-0.01	0	-0.01
8 (l)	-0.03	-0.01	+0.02	-0.01	+0.01
9	-0.05	-0.01	+0.04	-0.01	+0.03
18	+0.02	+0.03	+0.01	0	+0.01
19	-0.01	+0.01	+0.02	0	+0.02
1'	+0.45	+0.45	0	0	0
6'	+0.30	+0.28	-0.02	0	-0.02

(+)-Furospongin-1 β-fucofuranosides (**7a,b**)

Proton	$\Delta\delta_H{}^D$	$\Delta\delta_H{}^L$	$\Delta\Delta\delta_H$	$\Delta\delta_H{}^c$	$\Delta\delta_H{}^p$
6 (l)	+0.09	+0.01	-0.08	+0.01	-0.07
7 (l)	+0.17	+0.11	-0.06	+0.03	-0.03
9 (l)	+0.13	+0.03	-0.10	+0.01	-0.09
10a (l)[h]	+0.13	+0.14	+0.01	-0.17	-0.16
10b (l)[h]	+0.57	+0.24	-0.33	+0.14	-0.19
11	+0.21	+0.29	+0.08	-0.01	+0.07
12a (r)[h]	+0.07	+0.16	+0.09	-0.10	-0.01
12b (r)[h]	+0.12	+0.25	+0.13	-0.09	+0.04
13 (r)	+0.23	+0.55	+0.32	-0.05	+0.27
14 (r)	-0.01	+0.17	+0.18	-0.02	+0.16
15a (r)[h]	-0.03	+0.04	+0.07	+0.03	+0.10
15b (r)[h]	-0.03	+0.10	+0.13	-0.10	+0.03
16 (r)	-0.04	+0.07	+0.11	-0.03	+0.08
1'	+0.48	+0.50	+0.02	-0.02	0
6'	+0.28	+0.29	+0.01	0	+0.01

[a] For chemical shifts see Experimental Section. [b] The symbols (l) and (r) indicate the left and the right segments, respectively, to which the protons belong. [c] $\delta_{C5D5N}{}^D - \delta_{CDCl3}{}^D$. [d] $\delta_{C5D5N}{}^L - \delta_{CDCl3}{}^L$. [e] $\Delta\delta_H{}^L - \Delta\delta_H{}^D$. [f] $\delta_{CDCl3}{}^L - \delta_{CDCl3}{}^D$. [g] $\delta_{C5D5N}{}^L - \delta_{C5D5N}{}^D$. [h] Pro-*(R)* and pro-*(S)* assignments were unsuccessful.

4a,b and **5a,b**. In these compounds the influences of the unsymmetrical β-D- and β-L-furanosyl groups on the carbinyl proton are not equivalent. In the (*S*)-type furanosides **2a,b**, for example, irradiation at the anomeric proton caused larger NOE (6.6%) on the 3α-H of the β-D-isomer (**2a**), than that (4.5%) observed in the β-L-isomer (**2b**). Apparently, the glycosidic linkages are distorted to ease the steric hindrance. The ring-oxygen atom of the β-L-isomer must be situated considerably closer to the 3α-H, than is the oxygen atom in the β-D-isomer, causing a more deshielding effect (positive $\Delta\delta_H{}^p$ and $\Delta\delta_H{}^c$ values). The (*R*)-type glycosides **4a,b** and **5a,b** are subjected to the same influence, but in the opposite way, resulting in the negative $\Delta\delta_H{}^p$ and $\Delta\delta_H{}^c$ values for the carbinyl proton.

The symmetrically substituted fucofuranosides **7a,b** show significant $\Delta\delta_H{}^p$ value for 11-H (+0.07 ppm) but the $\Delta\delta_H{}^c$ value is negligible (-0.01 ppm, Table 1). Although the nomenclature is (11*R*), when the steric hindrances at γ-positions are taken into account, they correspond to (*S*)-type glycosides. The $\Delta\delta_H$ values indicate that the conformations of the two furanosyl groups of **7a,b** are symmetrical in $CDCl_3$ but they are unsymmetrical (*S*-type) in pyridine-d_5. This was supported by their ^{13}C NMR experiment (see below).

Pyridine-induced shielding effects

The solvated pyridine molecules also cause diamagnetic shielding regions for remote protons. Actually, in compounds **1a,b** to **7a,b**, the majority of the protons show negative p-shift values in one or both diastereomers (Table 1). Nevertheless, except for a few protons, their $\Delta\delta_H{}^p$ values are consistent with the configuration. The magnitudes of the inconsistent $\Delta\delta_H{}^p$ values are generally less than 0.02 ppm. This phenomenon indicates that, for the remote protons, the oxa-side shielding effects are relatively weaker than the oxy-side shielding effects. For example, the 5-H_2 and 10-H_3 of the two (-)-menthol β-fucofuranosides (**5a,b**) are more shielded in pyridine-d_5 relative to $CDCl_3$ (columns 2 and 3, Table 1). These protons (in the left segment) in the β-D-isomer suffer from smaller shielding than those in the β-L-isomer, resulting in the expected (negative) $\Delta\delta_H{}^p$ values.

^{13}C NMR Spectra for Determination of Absolute Configuration

The ^{13}C NMR spectra of the β-fucofuranosides **1a,b** to **7a,b** revealed simple but definite correlation with the configuration, which is a major advantage compared with the existing methods. Essentially the same results are obtained from the spectra measured in pyridine-d_5 and in $CDCl_3$. It has been known that the glycosidation of secondary alcohols causes specific glycosidation shift on the aglycon carbons. It is deshielding for the α-carbon but is shielding for the β-carbons, relative to the corresponding carbons of the starting alcohol. Kasai et al.[16a] and Tori et al.[16b] showed that, in both the α- and β-D-cyclohexylglucopyranoside derivatives, the β-methylene carbon which is *syn* to the oxa-side always experiences a smaller shielding β-effects (ca. - 2 ppm) than the other β-methylene carbon (ca. - 4 ppm) which is *syn* to the oxy-side. It has been found that the enantiomeric β-fucofuranosyl groups also cause these influences on the α- and two β-carbons of the aglycon.

General procedure and application

Subtraction of the chemical shifts, in the same way as in ^1H NMR, of the β-D-fucofuranoside from those of the corresponding carbons of the β-L-fucofuranoside affords significant $\Delta\delta_C$ values (in pyridine-d_5, $\Delta\delta_C{}^p$; in $CDCl_3$, $\Delta\delta_C{}^c$, Fig. 6). Cholesterol β-fucofuranosides (**1a,b**), when viewed as illustrated in Fig. 3, show negative $\Delta\delta_C{}^p$ value for the left β-carbon (C-2, -1.9 ppm) and positive $\Delta\delta_C{}^p$ value for the right β-carbon (C-4, +1.8 ppm), whereas they are negligible for the α- (C-3, +0.1 ppm) and anomeric (0 ppm) carbons. No appreciable differences from these values were observed from the spectra taken in $CDCl_3$. The same result was obtained for 5α-cholestan-3α-ol β-fucofuranosides (**6a,b**), indicating that the conformationally symmetrical β-D- and β-L-fucofuranosyl groups exert equivalent glycosidation shifts in the opposite way. The $\Delta\delta_C$ values at C-2 and C-4 in **1a,b** correspond to the difference of the magnitudes of the oxy- and oxa-side β-shift values.

The unsymmetrically substituted β-fucofuranosides showed a different but systematic pattern. In the (*S*)-type glycosides **2a,b** and **3a,b**, the $\Delta\delta_C$ values are significant and negative for the anomeric carbon (e.g, in

2a,b, $\Delta\delta_C{}^p$ -5.7 ppm), α-carbon (C-3, -5.4 ppm), and the left-hand β-carbon (C-2, -3.9 ppm), but it is quite small for the right-hand β-carbon (C-4, -0.7 ppm). In contrast, the $\Delta\delta_C$ values of the (*R*)-type glycosides (**4a,b** and **5a,b**) are significant and positive for the anomeric carbon (e.g, in **5a,b**, $\Delta\delta_C{}^p$ +5.3 ppm), α-carbon (C-3, + 4.9 ppm), and the right-hand β-carbon (C-2, +3.6 ppm), but it is small for the left-hand β-carbon (C-4, +0.8 ppm). The conformations of the furanosyl groups of **7a,b** were assumed to be different in $CDCl_3$ and in pyridine-d_5, from their $\Delta\delta_H{}^c$ and $\Delta\delta_H{}^p$ values (see above). The ^{13}C NMR experiment supports this assumption; the $\Delta\delta_C{}^c$ values are similar to those of the symmetrical glycosides **1a,b** and **6a,b**, whereas the $\Delta\delta_C{}^p$ values are similar to those of the unsymmetrical (*S*)-type glycosides **2a,b** and **3a,b** (Fig. 6).

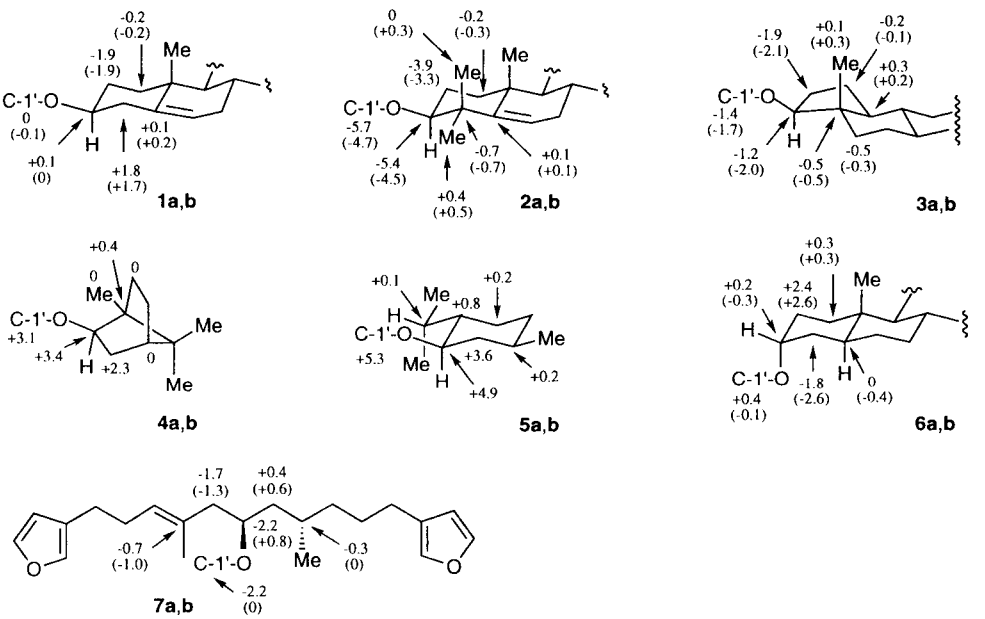


Fig. 6 The $\Delta\delta_C{}^p$ and $\Delta\delta_C{}^c$ (in parenthesis) values observed for the anomeric (C-1') and aglycon carbons of the β-D- and β-L-fucofuranoside derivatives of the chiral secondary alcohols **1** to **7** (100 MHz, in ppm).

Effects of the conformation of the β-fucofuranosidic linkages to the carbon chemical shifts

Beierbeck et al. showed that when two CH bonds adopt 1,3-synperiplanar alignment, large deshielding contribution (designated HC gauche interaction), by ca. +4.55 ppm, is incurred for both carbons.[17] They also showed that the effect of the non-bonded interaction of the δ-substituent is deshielding, rather than shielding as was believed previously.[18]

In the symmetrical glycosides **1a,b** and **6a,b**, the ring-oxygen atom of each furanosyl group should cause a deshielding δ-shift on the oxa-side β-carbon (Fig. 3), thereby partially cancelling (ca. 2 ppm) its shielding β-shift. In contrast, in the unsymmetrically substituted glycosides, the influences of the two enantiomeric furanosyl groups are not equivalent. Lemieux and Koto estimated the φ and ψ angles of the β-D-glucopyranosides of 2-methylcyclohexyl alcohols **8** [(1*S*, 2*S*)-isomer, φ = + 55°, ψ = - 10°] and **9** [(1*R*, 2*R*)-isomer, φ = + 55°, ψ = + 20°].[11] The antipode of the β-D-glucoside of **9** corresponds to the β-L-glucoside of **8** (φ = - 55°, ψ = - 20°).

When the ϕ and ψ angles estimated for the β-D- and β-L-glucosides of **8** are applied to the (*S*)-type furanosides **2a,b**, the relation between the anomeric proton and the 3α-proton would become closer in the β-D-isomer (Fig. 7, **2a**), but further detached from in the β-L-isomer (Fig. 7, **2b**), to the 1,3-synperiplanar alignment. Because of the HC gauche interaction, the C-1' and C-3 of the β-D-isomer (**2a**) are more deshielded than the corresponding carbons of the β-L-isomer (**2b**), resulting in the negative $\Delta\delta_C$ values. Simultaneously, the C-2 (left-hand β-carbon) in the β-D-isomer becomes closer to the ring-oxygen atom, but the C-2 in the β-L-isomer becomes closer to the anomeric proton; the deshielding δ-effect should increase in the β-D-isomer, also resulting in the negative $\Delta\delta_C$ value for C-2. In the β-L-isomer **2b**, the δ-effect has little influence on the C-4 quarternary carbon so that the difference in the C-4 chemical shifts becomes less significant. The (*R*)-type compounds **4a,b** and **5a,b** are subjected to these non-bonded interactions, but in the opposite way; this results in the positive $\Delta\delta_C$ values for the anomeric, α- and the right-hand β-carbons of **4a,b** and **5a,b**.

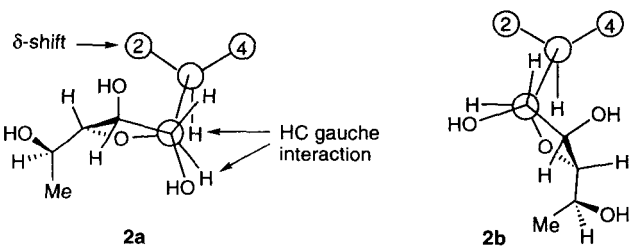


Fig. 7 Front view of the unsymmetrical conformations of the glycosidic linkages of the β-D- (**2a**, ϕ = +55°, ψ = -10°) and β-L-fucofuranoside (**2b**, ϕ = -55°, ψ = -20°) of the (*S*)-type secondary alcohol **2**.

If the $\Delta\delta_C$ values, regarding the carbinyl and anomeric carbons, are the result of their HC gauche interaction, then the magnitudes should be equivalent for these two carbons. Indeed, the $\Delta\delta_C$ values observed for the two carbons indicate an excellent agreement in both the (*S*)-type (e.g., $\Delta\delta_C{}^p$ - 5.7 and - 5.4 ppm in **2a,b**) and (*R*)-type glycosides (e.g., $\Delta\delta_C{}^p$ + 5.3 and + 4.9 ppm in **5a,b**, Figure 7).

The $\Delta\delta_C$ values in β-D- and β-L-glucopyranosides, and in β-D- and α-D-glucopyranosides

The same steric considerations should be applicable to the ^{13}C NMR of β-D- and β-L-glucopyranosides. Kasai *et al.* and Tori *et al.* reported the α- and two β-shift values of various glucopyranosides (in pyridine-d_5), together with the differences in the anomeric carbon chemical shifts relative to the corresponding methyl glucopyranoside.[16] Seo *et al.* correlated rather complicated combinations of the magnitudes of these four values with configurations.[19] As for the β-D- and β-L-glucopyranoside pairs, the data of the two compounds, 5α-cholestan-3β-ol and a triterpene dammarenediol-I, having 5α,6-dihydro A and B-rings of **1** and **2**, respectively, have been recorded.[16a] If we simply subtract the reported chemical shifts, for example, of the β-D-glucoside of 5α-cholestan-3β-ol [29.9 (C-2), 77.2 (C-3), 34.8 (C-4) and 102.0 ppm (C-1')] from the corresponding chemical shifts of the β-L-glucoside [28.3 (C-2), 77.7 (C-3), 36.5 (C-4) and 102.4 ppm (C-1')], the $\Delta\delta_C{}^p$ values woud be - 1.6 (C-2), + 0.5 (C-3), + 1.7 (C-4) and +0.4 ppm (C-1') (Fig. 8). These values, and those

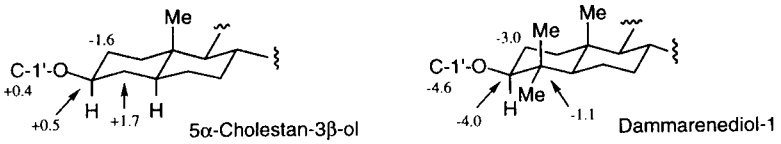


Fig. 8 The $\Delta\delta_C^p$ values (in ppm) obtained for the anomeric (C-1') and aglycon carbons, by subtracting the chemical shifts of the β-D-glucopyranoside from the corresponding chemical shifts of the β-L-glucopyranoside of 5α-cholestan-3β-ol and the triterpene dammarenediol-1.

also derived for dammarenediol-1 by the same treatment, correspond quite well to the $\Delta\delta_C^p$ values of **1a,b** and **2a,b**, respectively, derived by the fucofuranoside method (Fig. 6).

More important, this steric considerations are applicable even to the β-D- and α-D-glucopyranoside pair. According to Lemieux and Koto, the estimated ϕ angles of the β-D- and α-D-glucopyranosides of cyclohexyl alcohol and two 2-methylcyclohexyl alcohols (**8** and **9**) are constant (β-D, +55°; α-D, -60°).[11] These values show that the ϕ angle of the presumed β-L-glucopyranoside (-55°) is very close to that of the α-D-glucopyranoside (-60°). Similarly, the presumed ψ angles of the β-L-glucopyranosides are relatively close to the ψ angles of the corresponding α-D-glucopyranosides [cyclohexyl alcohol (β-L, - 10°; α-D, - 20°); **8** (β-L, - 20°; α-D, - 40°), **9** (β-L, + 10°; α-D, 0°)].[11] Thus, the spatial arrangement and mutual non-bonded interactions of the anomeric proton, ring-oxygen atom and carbinyl proton of β-L-glucopyranoside should be similar to those of the corresponding α-D-glucopyranoside (e.g., for cyclohexyl glucosides, Fig. 9).

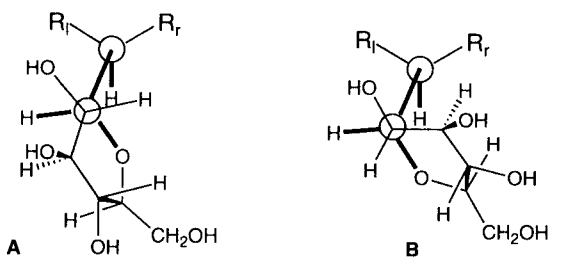


Fig. 9 Similar spatial arrangement of the anomeric proton, ring-oxygen atom and carbinyl proton of the β-L-glucopyranoside (**A**) and α-D-glucopyranoside (**B**) of cyclohexyl alcohol.

The anomeric carbon chemical shifts of β-D- and α-D-glucopyranosides are irrelevant to each other. However, their glycosidation shift values (relative to the C-1' signal of β-D- or α-D-glucopyranose) are virtually equivalent, if the aglycon exerts little interaction. If it can be assumed that the contribution of the HC gauche interaction (between the anomeric and carbonyl carbons) results in the difference in their glycosidation shift values, this difference can then be utilized as the $\Delta\delta_C$ value at C-1' of β-D- and α-D-glucopyranoside pair.

These assumptions were applied to the known β-D- and α-D-glucopyranosides pairs of nine secondary alcohols (**1**, **5**, **6**, **8** and **9**, and 5α-cholestan-3β-ol, (+)-menthol, and triterpenes smilagenin and methyl oleanoate).[16,19] The reported chemical shifts of the β-D-glucopyranoside of (-)-menthol (**5**), for example, are 41.1 (C-2), 77.0 (C-3) and 48.5 ppm (C-4), while the glycosidation shift of its anomeric carbon, relative to the C-1' of β-D-glucopyranose, is + 4.7 ppm. When these values are subtracted from the corresponding values of the α-D-glucopyranoside [43.6 (C-2), 81.1 (C-3) and 49.4 ppm (C-4), and the glycosidation shift +9.4 ppm (C-

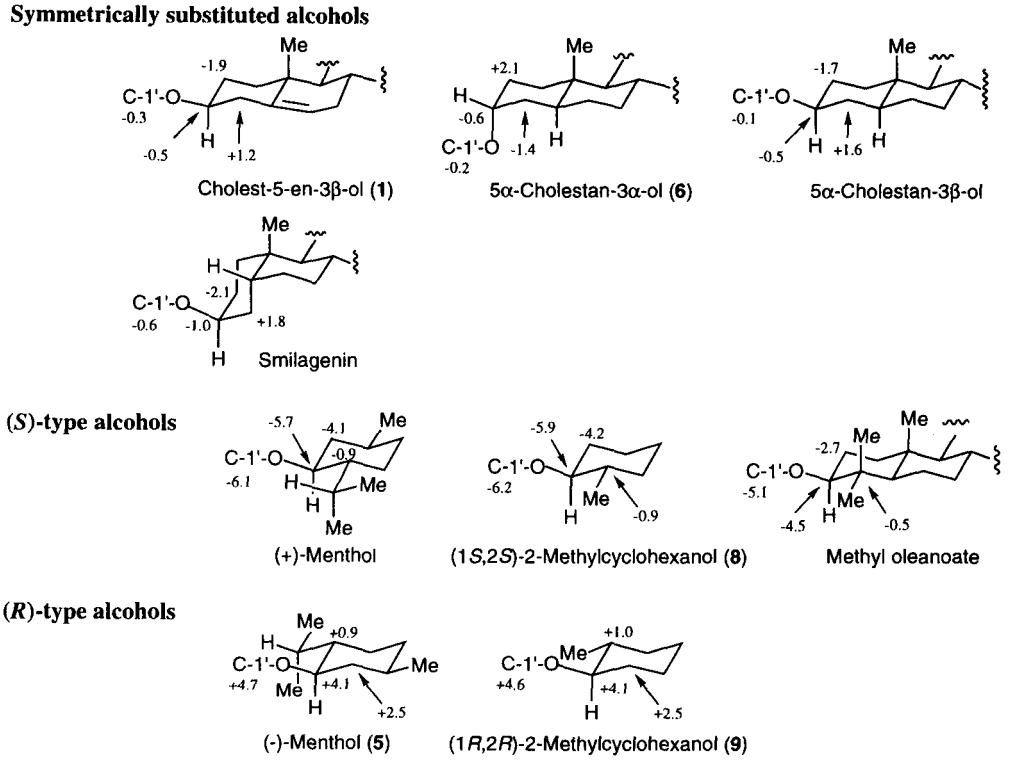


Fig. 10 The $\Delta\delta_C^P$ values (in ppm) calculated for the anomeric (C-1') and aglycon carbons, using the previously reported data of the β-D- and α-D-glucopyranoside pairs of secondary alcohols.

1')], the $\Delta\delta_C^P$ values woud be +2.5 (C-2), +4.1 (C-3), + 0.9 (C-4) and +4.7 ppm (C-1') (Fig. 10). These values correspond remarkably well to the $\Delta\delta_C^P$ values in Fig. 6, derived for **5a,b** by using the fucofuranoside method. The other eight compounds studied herein include symmetrically and unsymmetrically substituted alcohols, and alcohols having an axial or equatorial hydroxyl group. When their chemical shifts were treated in the same procedure as above, they showed, without exception, $\Delta\delta_C$ values which are consistent with an absolute configuration (Fig. 10). These results support the above hypotheses and show that, as regards the ^{13}C NMR spectra, the $\Delta\delta_C$ values derived from β-D- and β-L-glucopyranosides, and even from β-D- and α-D-glucopyranosides, can be used for predicting the absolute configuration of chiral secondary alcohols.

Conclusions

The fucofuranoside method affords evidences, from the ^1H and ^{13}C NMR spectra, for assigning the absolute configuration of secondary alcohols. The exo-anomeric effect of the glycosidic linkage secures the pertinent conformation, so that the method is applicable to the axially-oriented hydroxyl groups. For the chemical shifts, measured in pyridine-d_5, of the protons and carbons of the β-D- and β-L-fucofuranosides as illustrated in Fig. 3, the following generalizations were derived.

(*a*) In the ^1H NMR spectra, the $\Delta\delta_H^P$ values are positive for the protons of the right segment and negative for the protons of the left segment (Fig. 4).

(*b*) In the unsymmetrically substituted β-fucofuranosides, the $\Delta\delta_H^P$ value of the carbinyl proton is positive in the (*S*)-type glycosides (Fig. 4, **2a,b** and **3a,b**), whereas it is negative in the (*R*)-type glycosides (**4a,b** and **5a,b**).[20]

(*c*) In the ^{13}C NMR spectra, the $\Delta\delta_C^P$ values of the symmetrically substituted β-fucofuranosides are positive for the right-hand β-carbon and negative for the left-hand β-carbon, but they are negligible for the α- and anomeric carbons (Fig. 6, **1a,b** and **6a,b**).

(*d*) In the sterically unsymmetrical (*S*)-type β-fucofuranosides, the $\Delta\delta_C^P$ values of the anomeric carbon, α-carbon and the left-hand β-carbon are significant and negative, but they are small for the right-hand β-carbon (Fig. 6, **2a,b** and **3a,b**). In the (*R*)-type β-fucofuranosides, the $\Delta\delta_C^P$ values of the anomeric carbon, α-carbon and the right-hand β-carbon are significant and positive, but they are small for the left-hand β-carbon (Fig. 6, **4a,b** and **5a,b**).

The rules *b*, *c* and *d* are applicable to the spectra taken in $CDCl_3$. Also, the rules *c* and *d* are applicable to β-D- and β-L-glucopyranoside pairs (Fig. 8) and, with a certain modification regarding C-1', to β-D- and α-D-glucopyranoside pairs (Fig. 10).[21]

Experimental Section

General

Mps were determined on a Kofler hot stage and are uncorrected. The optical rotations were determined on a JASCO DIP-370 digital polarimeter. NMR spectra were determined on a JEOL JNM GX 400 spectrometer at 400 MHz (^1H) and at 100 MHz (^{13}C) and were referenced to the residual protons in the solvents (^1H: $CHCl_3$, 7.26 ppm; pyridine, 7.20 ppm) or the solvent carbons ($CDCl_3$ 77.03 ppm; pyridine-d_5 123.50 ppm) as internal standards. *J* values are given in Hz. Mass spectra were determined on a JEOL JMS DX 303 (EI) and JEOL JMS HX 110 (FAB) mass spectrometer. Flash column chromatography[22] was performed on silica gel (Wako gel C-300, 200-300 mesh, Wako Pure Chemical Industries).

D- and L-fucofuranose tetraacetates

D-fucose and L-fucose (2.5 g each) were individually dissolved in 100 ml of MeOH containing 0.8% HCl and kept at 15 °C for 4 d. The solution was neutralized by addition of excess $AgCO_3$, filtered, and the solvent was evaporated off. The residue was dissolved in 11 ml of pyridine and 9 mL of Ac_2O and kept at 0 °C overnight. The mixture was then added to ice-water and stirred for 1 h. It was extracted with $CHCl_3$ and the extract was thoroughly washed with saturated $NaHCO_3$ solution, H_2O and saturated NaCl solution, and then the solvent was evaporated giving a colorless viscous oil. It was dissolved in AcOH (17.5 ml) and Ac_2O (3.8 ml) and treated at -5 °C with conc. H_2SO_4 (0.8 ml), and kept at room temperature overnight. The mixture was added to ice-water, stirred, and then extracted with $CHCl_3$. The extract was washed with H_2O, saturated $NaHCO_3$ solution, H_2O and saturated NaCl solution, and the solvent was evaporated. The residue was an anomeric mixture of furanoside and pyranoside, of which the α- and β-fucofuranoside mixture is distinguishable by thin-layer chromatography (ethylacetate-benzene = 2:8) from that of the α- and β-fucopyranoside mixture which shows a higher mobility.[10d] A portion (1.5 g) of the mixture was subjected to flash chromatography over a

column of silica gel with 7.5% ethylacetate in benzene (900 ml) and 12% ethylacetate in benzene (400 ml) giving 460 mg of the pyranose tetraacetate mixture and then 860 mg of the furanose tetraacetate mixture. It is a ca. 3:1 mixture of β-anomer and α-anomer (^{1}H NMR, ref 10b) but gives the β-furanoside exclusively in the following glycosidation condition.

Preparation of β-D- and β-L-fucofuranosides

In a typical run, a mixture of the alcohol (0.052 mmol), fucofuranose tetraacetate (0.073 mmol) and 4A molecular sieve (150 mg) in dry CH_2Cl_2 (1 ml) and one drop of TMSOTf was stirred at room temperature for 30 min. Excess TMSOTf was quenched with one drop of triethylamine and the mixture was filtered. The filtrate was evaporated to dryness and dissolved in 1ml of MeOH and one drop of 28 % NaOMe in MeOH and kept for 30 min. After usual work-up, the mixture was subjected to flash chromatography over a column of silica gel with 2-4 % MeOH in $CHCl_3$ giving the β-glycoside. The yields were 60 % to quantitative, except for the labile furanoterpene furanosides **7a,b**, which partly decomposed during the process giving low yield of the products (33% and 35% for β-D- and β-L-isomers, respectively).

Cholest-5-en-3β-ol 3-*O*-β-D-fucofuranoside 1a. Mp 156-158 °C (from acetone); $[\alpha]^{23}_D$ - 66.2° (*c* 2.72, pyridine); δ_H (400 MHz, C_5D_5N) 0.67 (3H, s, 18-H_3), 0.97 (3H, s, 19-H_3), 1.65 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.74 (1H, m, 2β-H), 1.92 (1H, br d, *J* 17.5 Hz, 7β-H), 2.17 (1H, m, 2α-H), 2.39 (1H, br t, *J* 13.0 Hz, 4β-H), 2.55 (1H, ddd, *J* 13.0, 5.0, 2.0 Hz, 4α-H), 3.78 (1H, m, 3α-H), 5.33 (1H, m, 6-H), 5.68 (1H, d, *J* 2.0 Hz, 1'-H) [0.90 (9α-H), 1.01 (1α-H), 1.40 (8β-H), 1.56 (7α-H), 1.45 (11-H_2) and 1.75 (1β-H) detected by HSQC spectrum]; δ_H (400 MHz, $CDCl_3$) 0.67 (3H, s, 18-H_3), 1.00 (3H, s, 19-H_3), 1.34 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.84 (2H, m, 1β, 2α-H), 1.98 (1H, br d, *J* 17.5 Hz, 7β-H), 2.18 (1H, br t, *J* 12.0 Hz, 4β-H), 2.37 (1H, ddd, *J* 13.0, 5.0, 2.0 Hz, 4α-H), 3.56 (1H, m, 3α-H), 5.18 (1H, s, 1'-H), 5.36 (1H, m, 6-H) [0.90 (9α-H), 1.09 (1α-H), 1.45 (8β-H), 1.48 (11-H_2), 1.53 (7α-H) and 1.55 (2β-H) detected by HSQC spectrum]; δ_C (100 MHz, C_5D_5N) 12.0 (C-18), 19.5 (C-19), 20.5 (C-6'), 21.4 (C-11), 24.6 (C-15), 28.5 (C-16), 30.5 (C-2), 32.2 (C-8), 32.3 (C-7), 37.0 (C-10), 37.6 (C-1), 39.4 (C-4), 40.1 (C-12), 42.6 (C-13), 50.5 (C-9), 56.5 (C-17), 56.9 (C-14), 67.9 (C-5'), 77.2 (C-3), 79.3 (C-3'), 84.3 (C-2'), 88.2 (C-4'), 107.7 (C-1'), 121.8 (C-6), 141.1 (C-5); δ_C (100 MHz, $CDCl_3$) 11.9 (C-18), 19.4 (C-19), 20.3 (C-6'), 21.1 (C-11), 24.3 (C-15), 28.3 (C-16), 29.7 (C-2), 32.0 (C-8), 32.0 (C-7), 36.8 (C-10), 37.3 (C-1), 38.5 (C-4), 39.9 (C-12), 42.4 (C-13), 50.3 (C-9), 56.3 (C-17), 56.8 (C-14), 67.9 (C-5'), 76.4 (C-3), 79.1 (C-2', 3'), 90.4 (C-4'), 106.1 (C-1'), 122.2 (C-6), 140.3 (C-5); [Found (HRFABMS): MH^+, *m/z* 533.4199. $C_{33}H_{57}O_5$ requires 533.4206].

Cholest-5-en-3β-ol 3-*O*-β-L-fucofuranoside 1b. Mp 178-180 °C (from acetone); $[\alpha]^{23}_D$ +14.1°(*c* 3.82, pyridine); δ_H (400 MHz, C_5D_5N) 0.68 (3H, s, 18-H_3), 0.99 (3H, s, 19-H_3), 1.64 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.78 (1H, dt, *J* 13.5, 3.5 Hz, 1β-H), 1.93 (1H, dddd, *J* 17.5, 5.5, 5.5, 2.5 Hz, 7β-H), 2.00 (2H, m, 2α, 12β-H), 2.56 (1H, br t, *J* 13.5 Hz, 4β-H), 2.73 (1H, ddd, *J* 13.5, 5.0, 2.0 Hz, 4α-H), 3.78 (1H, m, 3α-H), 5.33 (1H, m, 6-H), 5.65 (1H, d, *J* 2.0 Hz, 1'-H) [0.93 (9α-H), 1.00 (1α-H), 1.42 (8β-H),1.46 (11-H_2), 1.57 (7α-H) and 1.60 (2β-H) detected by HSQC spectrum]; δ_H (400 MHz, $CDCl_3$) 0.68 (3H, s, 18-H_3), 1.00 (3H, s, 19-H_3), 1.35 (3H, d, *J* 6.5 Hz, 6'-H3), 1.87 (1H, dt, *J* 13.5, 3.5 Hz, 1β-H), 1.92 (1H, m, 2α-H), 1.98 (1H, m, 7β-H), 2.28 (1H, m, 4β-H), 2.30 (1H, 4α-H), 3.56 (1H, m, 3α-H), 5.18 (1H, s, 1'-H), 5.36 (1H, m, 6-H) [0.93 (9α-H), 1.05 (1α-H), 1.45 (2β, 8β-H), 1.48 (11-H_2) and 1.55 (7α-H) detected by HSQC spectrum];

δ_C (100 MHz, C_5D_5N) 12.0 (C-18), 19.5 (C-19), 20.6 (C-6'), 21.3 (C-11), 24.5 (C-15), 28.5 (C-16), 28.6 (C-2), 32.1 (C-8), 32.2 (C-7), 36.9 (C-10), 37.4 (C-1), 40.0 (C-12), 41.2 (C-4), 42.5 (C-13), 50.4 (C-9), 56.4 (C-17), 56.9 (C-14), 67.7 (C-5'), 77.3 (C-3), 79.2 (C-3'), 84.3 (C-2'), 88.1 (C-4'), 107.7 (C-1'), 121.8 (C-6), 141.2 (C-5); δ_C (100 MHz, $CDCl_3$) 11.9 (C-18), 19.4 (C-19), 20.3 (C-6'), 21.1 (C-11), 24.3 (C-15), 27.8 (C-2), 28.3 (C-16), 32.0 (C-8), 32.0 (C-7), 36.8 (C-10), 37.1 (C-1), 39.8 (C-12), 40.2 (C-4), 42.4 (C-13), 50.2 (C-9), 56.3 (C-17), 56.8 (C-14), 68.0 (C-5'), 76.4 (C-3), 79.1, 79.2 (C-2', 3'), 90.5 (C-4'), 106.0 (C-1'), 122.1 (C-6), 140.5 (C-5); [Found (HRFABMS): MH^+, *m/z* 533.4216. $C_{33}H_{57}O_5$ requires 533.4206].

4,4-Dimethylcholest-5-en-3β-ol 3-*O*-β-D-fucofuranoside 2a. Mp 167-170 °C (from acetone); $[\alpha]^{23}_D$ - 77.5° (*c* 3.64, pyridine); δ_H (400 MHz, C_5D_5N) 0.69 (3H, s, 18-H_3), 1.13 (3H, s, 19-H_3), 1.26 (3H, s, 4β-Me), 1.27 (3H, s, 4α-Me), 1.64 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.99 (1H, m, 2β-H), 2.08 (1H, dt, *J* 18.5, 5.5 Hz, 7β-H), 2.24 (1H, dq, *J* 13.5, 4.0 Hz, 2α-H), 3.32 (1H, dd, *J* 12.0, 4.0 Hz, 3α-H), 5.53 (1H, d, *J* 2.0 Hz, 1'-H), 5.59 (1H, dd, *J* 4.0, 3.0 Hz, 6-H) [0.91 (9α-H), 1.03 (1α-H), 1.44 (11-H_2), 1.49 (8β-H), 1.66 (1β-H) and 1.67 (7α-H) detected by HSQC spectrum]; δ_H (400 MHz, $CDCl_3$) 0.67 (3H, s, 18-H_3), 1.02 (3H, s, 4β-Me), 1.07 (3H, s, 19-H_3), 1.10 (3H, s, 4α-Me), 1.34 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.73 (1H, m, 1β-H), 1.90 (1H, br dq, *J* 13.0, 3.5 Hz, 2α-H), 2.09 (1H, ddd, *J* 18.5, 6.0, 5.0 Hz, 7β-H), 3.17 (1H, dd, *J* 11.5, 4.5 Hz, 3α-H), 5.08 (1H, s, 1'-H), 5.55 (1H, dd, *J* 4.5, 3.0 Hz, 6-H) [0.91 (9α-H), 1.10 (1α-H), 1.45 (11-H_2), 1.50 (8β-H), 1.62 (7α-H), 1.77 (2β-H) detected by HSQC spectrum]; δ_C (100 MHz, C_5D_5N) 12.1 (C-18), 20.5 (C-6'), 20.9 (C-11), 21.6 (C-19), 24.5 (C-15), 25.2 (4β-Me), 26.7 (C-2), 27.5 (4α-Me), 28.6 (C-16), 31.2 (C-8), 32.9 (C-7), 36.9 (C-10), 37.0 (C-1), 40.1 (C-12), 42.1 (C-4), 42.5 (C-13), 51.3 (C-9), 56.4 (C-17), 57.5 (C-14), 67.7 (C-5'), 79.2 (C-3'), 84.2 (C-2'), 85.9 (C-3), 87.9 (C-4'), 111.6 (C-1'), 120.2 (C-6), 150.5 (C-5); δ_C (100 MHz, $CDCl_3$) 11.9 (C-18), 20.3 (C-6'), 20.7 (C-11), 21.3 (C-19), 24.2 (C-15), 24.7 (4β-Me), 26.0 (C-2), 27.3 (4α-Me), 28.3 (C-16), 30.9 (C-8), 32.6 (C-7), 36.6 (C-10), 36.6 (C-1), 39.8 (C-12), 41.6 (C-4), 42.3 (C-13), 51.0 (C-9), 56.2 (C-17), 57.3 (C-14), 67.9 (C-5'), 78.7, 79.0 (C-2', 3'), 86.4 (C-3), 90.4 (C-4'), 110.2 (C-1'), 120.5 (C-6), 149.5 (C-5); [Found (HREIMS): M^+-H_2O, *m/z* 542.4315. $C_{35}H_{58}O_4$ requires 542.4335].

4,4-Dimethylcholest-5-en-3β-ol 3-*O*-β-L-fucofuranoside 2b. Mp 196-195 °C (from acetone); $[\alpha]^{23}_D$ + 20.5° (*c* 4.16, pyridine); δ_H (400 MHz, C_5D_5N) 0.70 (3H, s, 18-H_3), 1.13 (3H, s, 19-H_3), 1.29 (3H, s, 4β-Me), 1.44 (3H, s, 4α-Me), 1.62 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.93 (1H, dq, *J* 13.5, 3.5 Hz, 2α-H), 2.10 (1H, dt, *J* 18.5, 5.0 Hz, 7β-H), 3.57 (1H, dd, *J* 12.0, 5.5 Hz, 3α-H), 5.61 (1H, d, *J* 1.0 Hz, 1'-H), 5.66 (1H, br dd, *J* 4.0, 3.0 Hz, 6-H) [0.91 (9α-H), 0.98 (1α-H), 1.44 (11-H_2), 1.50 (8β-H), 1.68 (1β-H), 1.69 (7α-H) and 1.74 (2β-H) detected by HSQC spectrum]; δ_H (400 MHz, $CDCl_3$) 0.68 (3H, s, 18-H_3), 1.04 (3H, s, 4β-Me), 1.09 (3H, s, 19-H_3), 1.12 (3H, s, 4α-Me), 1.34 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.78 (1H, dt, *J* 13.5, 3.5 Hz, 1β-H), 1.83 (1H, m, 2α-H), 2.09 (1H, br dt, *J* 18.5, 5.0 Hz, 7β-H), 3.34 (1H, dd, *J* 11.5, 4.0 Hz, 3α-H), 5.17 (1H, s, 1'-H), 5.58 (1H, dd, *J* 5.0, 3.0 Hz, 6-H) [0.90 (9α-H), 1.06 (1α-H), 1.45 (11-H_2), 1.50 (8β-H), 1.62 (7α-H) and 1.68 (2β-H) detected by HSQC spectrum]; δ_C (100 MHz, C_5D_5N) 12.1 (C-18), 20.5 (C-6'), 21.0 (C-11), 21.6 (C-19), 22.8 (C-2), 24.5 (C-15), 25.2 (4β-Me), 27.9 (4α-Me), 28.6 (C-16), 31.3 (C-8), 32.9 (C-7), 36.8 (C-1), 37.0 (C-10), 40.1 (C-12), 41.4 (C-4), 42.5 (C-13), 51.2 (C-9), 56.4 (C-17), 57.6 (C-14), 67.6 (C-5'), 79.3 (C-3'), 80.5 (C-3), 84.3 (C-2'), 88.2 (C-4'), 105.9 (C-1'), 120.2 (C-6), 150.6 (C-5); δ_C (100 MHz, $CDCl_3$) 11.9 (C-18), 20.4 (C-6'), 20.7 (C-11), 21.3 (C-19), 22.7 (C-2), 24.2 (C-15), 25.0 (4β-

Me), 27.8 (4α-Me), 28.3 (C-16), 30.9 (C-8), 32.6 (C-7), 36.3 (C-1), 36.8 (C-10), 39.9 (C-12), 40.9 (C-4), 42.3 (C-13), 51.0 (C-9), 56.2 (C-17), 57.4 (C-14), 68.0 (C-5'), 79.2, 79.4 (C-2', 3'), 81.9 (C-3), 90.4 (C-4'), 105.5 (C-1'), 120.4 (C-6), 149.6 (C-5); [Found (HREIMS): M^+-H_2O, *m/z* 542.4333. $C_{35}H_{58}O_4$ requires 542.4335].

Androst-4-en-17β-ol-3-one 17-*O*-β-D-fucofuranoside 3a. Mp 178-180 °C (from acetone); $[\alpha]^{23}_D$ +8.5° (*c* 4.12, pyridine); δ_H (400 MHz, C_5D_5N) 0.72 (1H, dt, *J* 4.5, 11.5 Hz, 9α-H), 0.87 (3H, s, 18-H_3), 1.00 (3H, s, 19-H_3), 1.06 (1H, dt, *J* 4.5, 12.5 Hz, 12α-H), 1.19 (1H, dq, *J* 6.0, 12.0 Hz, 15β-H), 1.26 (1H, dq, *J* 3.5, 12.5 Hz, 11β-H), 1.45 (1H, m, 15α-H), 1.63 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.81 (1H, m, 16β-H), 1.90 (1H, dt, *J* 12.5, 3.0 Hz, 12β-H), 2.15 (1H, m, 16α-H), 3.72 (1H, t, *J* 8.5 Hz, 17α-H), 5.52 (1H, d, *J* 2.0 Hz, 1'-H), 5.84 (1H, br s, 4-H) [0.79 (14α-H), 0.81(7α-H), 1.35 (11α-H), 1.37 (8β-H), 1.62 (7β-H) detected by HSQC spectrum]; δ_H (400 MHz, $CDCl_3$) 0.76 (3H, s, 18-H_3), 1.17 (1H, m, 12α-H), 1.18 (3H, s, 19-H_3), 1.33 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.42 (1H, dq, *J* 3.5, 12.5 Hz, 11β-H), 1.88 (1H, dt, *J* 12.5, 3.5 Hz, 12β-H), 2.08 (1H, m, 16α-H), 3.58 (1H, t, *J* 8.5 Hz, 17α-H), 5.06 (1H, s, 1'-H), 5.72 (1H, br s, 4-H) [0.92 (9α-H), 0.98 (14α-H), 1.00 (7α-H), 1.29 (15β-H), 1.52 (16β-H), 1.55 (8β-H), 1.58 (11α-H), 1.61 (15α-H) and 1.84 (7β-H) detected by HSQC spectrum]; δ_C (100 MHz, C_5D_5N) 12.0 (C-18), 17.2 (C-19), 20.5 (C-6'), 20.8 (C-11), 23.6 (C-15), 29.8 (C-16), 31.8 (C-7), 32.7 (C-6), 34.3 (C-2), 35.4 (C-8), 35.9 (C-1), 37.5 (C-12), 38.7 (C-10), 43.1 (C-13), 50.5 (C-14), 54.1 (C-9), 67.6 (C-5'), 79.4 (C-3'), 84.1 (C-2'), 87.3 (C-17), 88.1 (C-4'), 109.8 (C-1'), 124.1 (C-4), 170.4 (C-5), 198.2 (C-3); δ_C (100 MHz, $CDCl_3$) 11.7 (C-18), 17.4 (C-19), 20.2 (C-6'), 20.6 (C-11), 23.4 (C-15), 29.1 (C-16), 31.5 (C-7), 32.8 (C-6), 33.9 (C-2), 35.5 (C-8), 35.8 (C-1), 37.1 (C-12), 38.7 (C-10), 42.8 (C-13), 50.3 (C-14), 53.9 (C-9), 67.7 (C-5'), 78.7, 79.0 (C-2', 3'), 87.1 (C-17), 90.6 (C-4'), 108.6 (C-1'), 123.9 (C-4), 171.2 (C-5), 199.6 (C-3); [Found (HRFABMS): MH^+, *m/z* 435.2754. $C_{25}H_{39}O_6$ requires 435.2747].

Androst-4-en-17β-ol-3-one 17-*O*-β-L-fucofuranoside 3b. Mp 157-159 °C (from acetone); $[\alpha]^{23}_D$ +123° (*c* 3.98, pyridine); δ_H (400 MHz, C_5D_5N) 0.89 (3H, s, 18-H_3), 1.01 (3H, s, 19-H_3), 1.07 (1H, dt, *J* 4.5, 13.0 Hz, 12α-H), 1.20 (1H, dq, *J* 6.0, 12.0 Hz, 15β-H), 1.65 (3H, d, *J* 6.5 Hz, 6'-H_3), 2.01 (1H, m, 16α-H), 2.14 (1H, dt, *J* 13.0, 3.0 Hz, 12β-H), 3.77 (1H, t, *J* 8.5 Hz, 17α-H), 5.44 (1H, br s, 1'-H), 5.84 (1H, br s, 4-H) [0.73 (9α-H), 0.79 (14α-H), 0.82 (7α-H), 1.28 (11β-H), 1.37 (11α-H), 1.39 (8β-H), 1.45 (15α-H), 1.61 (16β-H) and 1.62 (7β-H) detected by HSQC spectrum]; δ_H (400 MHz, $CDCl_3$) 0.75 (3H, s, 18-H_3), 0.92 (1H, ddd, *J* 12.5, 11.0, 4.0 Hz, 9α-H), 1.15 (1H, dt, *J* 4.5, 12.5 Hz, 12α-H), 1.18 (3H, s, 19-H_3), 1.33 (3H, d, *J* 6.5 Hz, 6'-H_3), 2.07 (1H, m, 16α-H), 3.68 (1H, t, *J* 8.5 Hz, 17α-H), 5.01 (1H, s, 1'-H), 5.72 (1H, br s, 4-H) [1.00 (7α, 14α-H), 1.32 (15β-H), 1.40 (11β-H), 1.51 (16β-H), 1.57 (8β-H), 1.58 (11α-H), 1.64 (15α-H) and 1.83 (7β, 12β-H) detected by HSQC spectrum]; δ_C (100 MHz, C_5D_5N) 12.1 (C-18), 17.2 (C-19), 20.6 (C-6'), 20.8 (C-11), 23.4 (C-15), 27.9 (C-16), 31.8 (C-7), 32.8 (C-6), 34.4 (C-2), 35.5 (C-8), 35.9 (C-1), 37.0 (C-12), 38.8 (C-10), 42.6 (C-13), 50.8 (C-14), 54.2 (C-9), 67.6 (C-5'), 79.2 (C-3'), 84.3 (C-2'), 86.1 (C-17), 88.1 (C-4'), 108.4 (C-1'), 124.1 (C-4), 170.5 (C-5), 198.3 (C-3); δ_C (100 MHz, $CDCl_3$) 12.0 (C-18), 17.4 (C-19), 20.2 (C-6'), 20.6 (C-11), 23.5 (C-15), 27.0 (C-16), 31.5 (C-7), 32.8 (C-6), 33.9 (C-2), 35.5 (C-8), 35.8 (C-1), 36.8 (C-12), 38.7 (C-10), 42.3 (C-13), 50.5 (C-14), 54.0 (C-9), 67.7 (C-5'), 78.8, 79.0 (C-2', 3'), 85.1 (C-17), 90.5 (C-4'), 106.9 (C-1'), 123.9 (C-4), 171.2 (C-5), 199.6 (C-3); [Found (HRFABMS): MH^+, *m/z* 435.2740. $C_{25}H_{39}O_6$ requires 435.2747].

[(1*S*)-*endo*]-(-)-Borneol 2-*O*-β-D-fucofuranoside 4a. Mp 100-101 °C (from acetone); $[\alpha]^{23}_D$ - 96.3° (*c* 3.22, pyridine); δ_H (400 MHz, C_5D_5N) 0.76 (3H, s, 8-H_3), 0.80 (9-H_3), 0.99 (10-H_3), 1.13 (1H, dd, *J* 13.0, 3.5 Hz, 3-*endo*), 1.22 (1H, m, 5-*endo*), 1.24 (1H, m, 6-*exo*), 1.56 (1H, t, *J* 4.5 Hz, 4-H), 1.60 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.67 (1H, m, 5-*exo*), 2.13 (1H, m, 3-*exo*), 2.26 (1H, m, 6-*endo*), 4.22 (1H, dt, *J* 8.5, 2.5 Hz, 2-*exo*), 5.45 (1H, s, 1'-H); δ_H (400 MHz, $CDCl_3$) 0.84 (3H, s, 10-H_3), 0.86 (3H, s, 9-H_3), 0.87 (3H, s, 8-H_3), 1.03 (1H, dd, *J* 13.5, 3.5 Hz, 3-*endo*), 1.22 (1H, m, 5-*endo*), 1.24 (1H, m, 6-*exo*), 1.34 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.68 (1H, m, 4-H), 1.72 (1H, m, 5-*exo*), 1.78 (1H, m, 6-*endo*), 2.17 (1H, m, 3-*exo*), 4.05 (2H, m, 2-exo, 5'-H), 5.04 (1H, s, 1'-H); δ_C (100 MHz, C_5D_5N) 13.9 (C-10), 18.9 (C-8), 19.9 (C-9), 20.5 (C-6'), 27.2 (C-6), 28.6 (C-5), 36.1 (C-3), 45.4 (C-4), 47.9 (C-7), 49.2 (C-1), 67.6 (C-5'), 79.2 (C-3'), 80.9 (C-2), 84.3 (C-2'), 88.0 (C-4'), 107.7 (C-1'); [Found (HRFABMS): MH^+, *m/z* 301.2002. $C_{16}H_{29}O_5$ requires 301.2015].

[(1*S*)-*endo*]-(-)-Borneol 2-*O*-β-L-fucofuranoside 4b. Mp 91-92 °C (from acetone); $[\alpha]^{23}_D$ + 53.2° (*c* 4.44, pyridine); δ_H (400 MHz, C_5D_5N) 0.79 (6H, s, 8, 9-H_3), 0.88 (10-H_3), 1.20 (1H, m, 6-*exo*), 1.27 (1H, m, 5-*endo*), 1.42 (1H, dd, *J* 13.5, 3.5 Hz, 3-*endo*), 1.55 (1H, br t, *J* 4.5 Hz, 4-H), 1.60 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.66 (1H, m, 5-*exo*), 2.24 (1H, m, 6-*endo*), 2.31 (1H, m, 3-*exo*), 3.99 (1H, ddd, *J* 10.0, 3.0, 2.0 Hz, 2-*exo*), 5.47 (1H, d, *J* 2.0 Hz, 1'-H); δ_H (400 MHz, $CDCl_3$) 0.85 (3H, s, 10-H_3), 0.86 (3H, s, 9-H_3), 0.87 (3H, s, 8-H_3), 1.02 (1H, dd, *J* 13.5, 3.5 Hz, 3-*endo*), 1.17 (1H, m, 5-*endo*), 1.25 (1H, m, 6-*exo*), 1.34 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.63 (1H, br t, *J* 4.5 Hz, 4-H), 1.71 (1H, m, 5-*exo*), 1.77 (1H, m, 6-*endo*), 2.28 (1H, m, 3-*exo*), 3.83 (1H, ddd, *J* 10.0, 3.5, 2.5 Hz, 2-*exo*), 5.03 (1H, s, 1'-H) ; δ_C (100 MHz, C_5D_5N) 13.9 (C-10), 18.9 (C-8), 19.8 (C-9), 20.5 (C-6'), 27.2 (C-6), 28.6 (C-5), 38.4 (C-3), 45.4 (C-4), 47.5 (C-7), 49.6 (C-1), 67.5 (C-5'), 79.3 (C-3'), 84.1 (C-2'), 84.3 (C-2), 87.9 (C-4'), 110.8 (C-1'); [Found (HRFABMS): MH^+, *m/z* 301.1991. $C_{16}H_{29}O_5$ requires 301.2015].

(-)-Menthol 3-*O*-β-D-fucofuranoside 5a. Mp 134-135 °C (from acetone); $[\alpha]^{23}_D$ - 150° (*c* 2.54, pyridine); δ_H (400 MHz, C_5D_5N) 0.76 (1H, m, 6β-H), 0.81 (3H, d, *J* 7.0 Hz, 7-H_3), 0.86 (1H, br q, *J* 11.5 Hz, 2β-H), 0.89 (3H, d, *J* 7.0 Hz, 10-H_3), 0.94 (1H, m, 5α-H), 0.96 (3H, d, *J* 7.0 Hz, 9-H_3), 1.19 (1H, m, 1α-H), 1.33 (1H, ddt, *J* 12.5, 10.5, 2.5 Hz, 4β-H), 1.56 (2H, br d, *J* 11.0 Hz, 5β, 6α-H), 1.63 (3H, d, *J* 6.5 Hz, 6'-H_3), 2.13 (1H, m, br d, *J* 12.0 Hz, 2α-H), 2.58 (1H, d sept, *J* 2.0, 7.0 Hz, 8-H), 3.66 (1H, dt, *J* 2.0, 7.0 Hz, 3α-H), 5.59 (1H, d, *J* 2.0 Hz, 1'-H); δ_H (400 MHz, $CDCl_3$) 0.80 (3H, d, *J* 7.0 Hz, 9-H_3), 0.87 (1H, m, 2β-H), 0.88 (1H, m, 6β-H), 0.90 (3H, d, *J* 7.0 Hz, 7-H_3), 0.93 (3H, d, *J* 7.0 Hz, 10-H_3), 0.99 (1H, dq, *J* 3.0, 13.0 Hz, 5α-H), 1.23 (1H, m, 4β-H), 1.34 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.38 (1α-H, m, 1α-H), 1.65 (1H, m, 5β-H), 1.67 (1H, m, 6α-H), 2.00 (1H, d sept, *J* 3.0, 7.0 Hz, 8-H), 2.10 (1H, br d, *J* 12.5 Hz, 2α-H), 3.53 (1H, dt, *J* 4.0, 10.5 Hz, 3α-H), 5.18 (1H, s, 1'-H); δ_C (100 MHz, C_5D_5N) 16.1 (C-9), 20.6 (C-6'), 21.3 (C-10), 22.4 (C-7), 23.5 (C-5), 25.7 (C-8), 31.6 (C-1), 34.8 (C-6), 40.4 (C-2), 48.4 (C-4), 67.4 (C-5'), 74.7 (C-3), 79.3 (C-3'), 84.4 (C-2'), 88.1 (C-4'), 105.5 (C-1'); [Found (HRFABMS): MH^+, *m/z* 303.2170. $C_{16}H_{31}O_5$ requires 303.2171].

(-)-Menthol 3-*O*-β-L-fucofuranoside 5b. Mp 66-67 °C (from acetone); $[\alpha]^{23}_D$ + 32.9° (*c* 1.58, pyridine); δ_H (400 MHz, C_5D_5N) 0.76 (1H, m, 6β-H), 0.77 (3H, d, *J* 7.0 Hz, 9-H_3), 0.81 (3H, d, *J* 7.0 Hz,

7-H_3), 0.83 (3H, d, *J* 7.0 Hz, 10-H_3), 0.90 (1H, dq, *J* 3.5, 12.5 Hz, 5α-H), 1.18 (1H, br q, *J* 11.5 Hz, 2β-H), 1.27 (1H, m, 1α-H), 1.32 (1H, ddt, *J* 12.0, 10.5, 3.0 Hz, 4β-H), 1.52 (1H, m, 5β-H), 1.54 (1H, m, 6α-H), 1.62 (3H, d, *J* 6.5 Hz, 6'-H_3), 2.39 (1H, d sept, *J* 2.0, 7.0 Hz, 8-H), 2.48 (1H, m, 2α-H), 3.49 (1H, dt, *J* 4.5, 10.5 Hz, 3α-H), 5.54 (1H, d, *J* 2.0 Hz, 1'-H); δ_H (400 MHz, $CDCl_3$) 0.79 (3H, d, *J* 7.0 Hz, 9-H_3), 0.82 (1H, m, 6β-H), 0.90 (6H, d, *J* 7.0 Hz, 7, 10-H_3), 0.96 (1H, m, 2β-H), 0.98 (1H, m, 5α-H), 1.18 (1H, ddt, *J* 12.0, 10.0, 3.0 Hz, 4β-H), 1.36 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.43 (1H, m, 1α-H), 1.62 (1H, m, 5β-H), 1.65 (1H, m, 6α-H), 2.07 (1H, m, 8-H), 2.12 (1H, m, 2α-H), 3.39 (1H, dt, *J* 4.5, 10.5 Hz, 3α-H), 5.10 (1H, s, 1'-H); δ_C (100 MHz, C_5D_5N) 16.5 (C-9), 20.4 (C-6'), 21.2 (C-10), 22.5 (C-7), 23.7 (C-5), 25.8 (C-8), 31.8 (C-1), 34.7 (C-6), 44.0 (C-2), 49.2 (C-4), 67.7 (C-5'), 79.2 (C-3'), 79.6 (C-3), 84.1 (C-2'), 88.1 (C-4'), 110.8 (C-1'); [Found (HRFABMS): MH^+, *m/z* 303.2161. $C_{16}H_{31}O_5$ requires 303.2171].

5α-Cholestan-3α-ol 3-*O*-β-D-fucofuranoside 6a. Mp 152.5-153.5 °C (from acetone); $[\alpha]^{23}_D$ - 22.1° (*c* 3.48, pyridine); δ_H (400 MHz, C_5D_5N) 0.66 (3H, s, 18-H_3), 0.76 (3H, s, 19-H_3), 1.64 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.87 (1H, br d, *J* 14.0 Hz, 2α-H), 4.10 (1H, br s, 3β-H), 5.57 (1H, d, *J* 2.0 Hz, 1'-H) [0.64 (9α-H), 0.89 (7α-H), 1.18 (6β-H), 1.23 (6α and 11β-H), 1.30 (8β-H), 1.37 (1-H_2), 1.45 (4β and 11α-H), 1.48 (2β-H), 1.62 (7β-H) and 1.80 (4α and 5α-H) detected by HSQC spectrum]; δ_H (400 MHz, $CDCl_3$) 0.64 (3H, s, 18-H_3), 0.77 (3H, s, 19-H_3), 1.34 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.76 (1H, br d, *J* 14.5 Hz, 2α-H), 3.97 (1H, br t, *J* 2.5 Hz, 3β-H), 5.12 (1H, s, 1'-H) [0.69 (9α-H), 0.88 (7α-H), 1.14 (1α-H), 1.17 (6-H_2), 1.23 (11β-H), 1.33 (8β-H), 1.37 (5α-H), 1.44 (1β-H), 1.46 (4-H_2), 1.47 (11α-H), 1.53 (2β-H) and 1.64 (7β-H) detected by HSQC spectrum]; δ_C (100 MHz, C_5D_5N) 11.7 (C-19), 12.3 (C-18), 20.6 (C-6'), 21.1 (C-11), 24.4 (C-15), 25.8 (C-2), 28.5 (C-16), 28.9 (C-6), 32.3 (C-7), 33.0 (C-1), 35.0 (C-4), 35.6 (C-8), 36.1 (C-10), 39.9 (C-5), 40.3 (C-12), 42.8 (C-13), 54.4 (C-9), 56.6 (C-14, 17), 67.5 (C-5'), 72.3 (C-3), 79.1 (C-3'), 84.5 (C-2'), 87.8 (C-4'), 107.6 (C-1'); δ_C (100 MHz, $CDCl_3$) 11.4 (C-19), 12.1 (C-18), 20.3 (C-6'), 20.8 (C-11), 24.2 (C-15), 25.2 (C-2), 28.3 (C-16), 28.6 (C-6), 32.0 (C-7), 32.7 (C-1), 34.6 (C-4), 35.6 (C-8), 36.0 (C-10), 40.1 (C-5, 12), 42.6 (C-13), 54.4 (C-9), 56.4, 56.5 (C-14, 17), 67.9 (C-5'), 72.1 (C-3), 78.9, 79.2 (C-2', 3'), 90.5 (C-4'), 106.2 (C-1'); [Found (HRFABMS): MH^+, *m/z* 535.4360. $C_{33}H_{59}O_5$ requires 535.4362].

5α-Cholestan-3α-ol 3-*O*-β-L-fucofuranoside 6b. Mp 133-135 °C (from acetone); $[\alpha]^{23}_D$ + 54.6° (*c* 3.58, pyridine); δ_H (400 MHz, C_5D_5N) 0.67 (3H, s, 18-H_3), 0.78 (3H, s, 19-H_3), 1.62 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.70 (1H, m, 5α-H), 2.06 (1H, br d, *J* 13.0 Hz, 2α-H), 4.10 (1H, br s, 3β-H), 5.57 (1H, d, *J* 2.0 Hz, 1'-H) [0.67 (9α-H), 0.82 (7α-H), 1.10 (12α-H), 1.15 (6-H_2), 1.24 (11β-H), 1.31 (8β-H), 1.36 (4β-H), 1.45 (1β-H), 1.49 (11α-H), 1.55 (1α-H), 1.61 (7β-H), 1.63 (2β-H) and 1.64 (4α-H) detected by HSQC spectrum]; δ_H (400 MHz, $CDCl_3$) 0.64 (3H, s, 18-H_3), 0.77 (3H, s, 19-H_3), 1.34 (3H, d, *J* 6.5 Hz, 6'-H_3), 3.96 (1H, br t, *J* 3.0 Hz, 3β-H), 5.12 (1H, s, 1'-H) [0.68 (9α-H), 0.89 (7α-H), 1.15 (1α-H), 1.18 (6-H_2), 1.23 (11β-H), 1.32 (8β-H), 1.35 (4β, 5α-H), 1.46 (1β, 11α-H), 1.47 (4α-H), 1.64 (7β-H) and 1.66 (2-H_2) detected by HSQC spectrum]; δ_C (100 MHz, C_5D_5N) 11.7 (C-19), 12.3 (C-18), 20.5 (C-6'), 21.1 (C-11), 24.4 (C-15), 28.2 (C-2), 28.6 (C-16), 29.0 (C-6), 32.3 (C-7), 33.2 (C-4), 33.3 (C-1), 35.7 (C-8), 36.2 (C-10), 39.9 (C-5), 40.3 (C-12), 42.9 (C-13), 54.4 (C-9), 56.7 (C-14, 17), 67.8 (C-5'), 72.5 (C-3), 79.3 (C-3'), 84.3 (C-2'), 88.1 (C-4'), 108.0 (C-1'); δ_C (100 MHz, $CDCl_3$) 11.4 (C-19), 12.1 (C-18), 20.3 (C-6'), 20.8 (C-11), 24.2 (C-15), 27.8 (C-2), 28.3 (C-16), 28.5 (C-6), 32.0 (C-4, 7), 33.0 (C-1), 35.5 (C-8), 35.9 (C-10), 39.7 (C-5),

40.0 (C-12), 42.6 (C-13), 54.2 (C-9), 56.3, 56.5 (C-14, 17), 67.8 (C-5'), 71.8 (C-3), 78.7, 79.2 (C-2', 3'), 90.5 (C-4'), 106.1 (C-1'); [Found (HRFABMS): MH^+, *m/z* 535.4353. $C_{33}H_{59}O_5$ requires 535.4362].

(+)-Furospongin-1 11-*O*-β-D-fucofuranoside 7a. Colorless oil; $[\alpha]^{23}_D$ - 21.9° (*c* 3.80, pyridine); δ_H (400 MHz, C_5D_5N) 0.90 (3H, d, *J* 6.5 Hz, 14-H_3), 1.17 (1H, m, 15a-H), 1.53 (2H, br m, 16-H_2), 1.61 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.65 (1H, m, 12b-H), 1.74 (3H, s, 9-H_3), 1.80 (1H, m, 13-H), 2.69 (1H, dd, *J* 13.0, 6.0 Hz, 10b-H), 4.10 (1H, m, 11-H), 5.36 (1H, br t, *J* 7.0 Hz, 7-H), 5.58 (1H, br s, 1'-H), 6.39, 6.42 (each 1H, br s, 2, 19-H), 7.43, 7.55 (each 1H, br s, 4, 21-H), 7.55 (2H, m, 1, 20-H) [1.29 (12a-H), 1.30 (15b-H), 2.34 (10a-H), 2.35 (16, 17-H_2) and 2.52 (5-H_2) detected by HSQC spectrum]; δ_H (400 MHz, $CDCl_3$) 0.91 (3H, d, *J* 6.5 Hz, 14-H_3), 1.33 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.61 (3H, s, 9-H_3), 2.12 (1H, dd, *J* 13.5, 5.0 Hz, 10b-H), 2.21 (1H, dd, *J* 13.5, 8.5 Hz, 10a-H), 3.89 (1H, m, 11-H), 5.10 (1H, s, 1'-H), 5.19 (1H, br t, *J* 6.5 Hz, 7-H), 6.27 (2H, br s, 2, 19-H), 7.20, 7.21 (each br s, 4, 21-H), 7.33, 7.34 (each br t, *J* 2.0 Hz, 1, 20-H) [1.20 (15a-H), 1.22 (12a-H), 1.33 (15b-H), 1.53 (12b-H), 1.57 (16-H_2 and 13-H) and 2.26 (6-H_2) detected by HSQC spectrum]; δ_C (100 MHz, C_5D_5N) 16.6 (C-9), 19.9 (C-14), 20.6 (C-6'), 25.2 (C-5, 17), 27.7 (C-16), 28.9 (C-6), 29.2 (C-13), 37.6 (C-15), 42.3 (C-12), 47.3 (C-10), 67.4 (C-5'), 74.7 (C-11), 79.2 (C-3'), 83.9 (C-2'), 88.4 (C-4'), 109.4 (C-1'), 111.7 (C-2, 19), 125.5, 125.8 (C-3, 18), 126.9 (C-7), 133.7 (C-8), 139.4, 139.5 (C-4, 21), 143.2 (C-1, 20); δ_C (100 MHz, $CDCl_3$) 15.7 (C-9), 20.2 (C-6'), 20.4 (C-14), 24.8, 25.0 (C-5, 17), 27.2 (C-16), 28.5 (C-6), 29.2 (C-13), 36.7 (C-15), 41.6 (C-12), 46.5 (C-10), 67.9 (C-5'), 72.5 (C-11), 78.8, 79.1 (C-2', 3'), 90.6 (C-4'), 106.6 (C-1'), 111.0 (C-2, 19), 124.8, 125.1 (C-3, 18), 127.2 (C-7), 133.1 (C-8), 138.8, 138.9 (C-4, 21), 142.6, 142.7 (C-1, 20); [Found (HRFABMS): MH^+, *m/z* 477.2842. $C_{27}H_{41}O_7$ requires 477.2852].

(+)-Furospongin-1 11-*O*-β-L-fucofuranoside 7b. Colorless oil; $[\alpha]^{23}_D$ + 56.7° (*c* 4.02, pyridine); δ_H (400 MHz, C_5D_5N) 1.06 (3H, d, *J* 6.5 Hz, 14-H_3), 1.62 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.65 (3H, s, 9-H_3), 2.07 (1H, m, 13-H), 2.18 (1H, dd, *J* 13.0, 7.5 Hz, 10a-H), 2.28 (2H, br q, *J* 7.5 Hz, 6-H_2), 2.41 and 2.49 (each 2H, br t, *J* 7.0 Hz, 5, 17-H_2), 4.17 (1H, m, 11-H), 5.33 (1H, br t, *J* 7.0 Hz, 7-H), 5.58 (1H, d, *J* 1.5 Hz, 1'-H), 6.40 (2H, br s, 2, 19-H), 7.44, 7.45 (each 1H, br s, 4, 21-H), 7.54 (2H, m, 1, 20-H) [1.27 (15a-H), 1.28 (12a-H), 1.33 (15b-H), 1.61 (16-H_2), 1.69 (12b-H) and 2.50 (10b-H) detected by HSQC spectrum]; δ_H (400 MHz, $CDCl_3$) 0.89 (3H, d, *J* 6.5 Hz, 14-H_3), 1.12 (1H, ddd, *J* 13.5, 10.0, 3.5 Hz, 12a-H), 1.33 (3H, d, *J* 6.5 Hz, 6'-H_3), 1.44 (1H, ddd, *J* 13.5, 10.0, 4.0 Hz, 12b-H), 1.62 (3H, s, 9-H_3), 2.04 (1H, dd, *J* 13.5, 7.0 Hz, 10a-H), 2.27 (2H, br q, *J* 7.5 Hz, 6-H_2), 2.38 and 2.47 (each 2H, br q, *J* 7.5 Hz, 5, 17-H_2), 3.88 (1H, m, 11-H), 5.08 (1H, s, 1'-H), 5.22 (1H, br t, *J* 7.0 Hz, 7-H), 6.25, 6.27 (each 1H, br s, 2, 19-H), 7.21 (2H, br s, 4, 21-H), 7.33 (2H, br s, 1, 20-H) [1.23 (15-H_2), 1.52 (13-H), 1.54 (16-H_2) and 2.26 (10b-H) detected by HSQC spectrum]; δ_C (100 MHz, C_5D_5N) 16.7 (C-9), 19.3 (C-14), 20.7 (C-6'), 25.1, 25.2 (C-5, 17), 27.9 (C-16), 28.8 (C-6), 28.9 (C-13), 37.9 (C-15), 42.7 (C-12), 45.6 (C-10), 67.3 (C-5'), 72.5 (C-11), 79.3 (C-3'), 84.2 (C-2'), 88.4 (C-4'), 107.2 (C-1'), 111.7 (C-2, 19), 125.4, 125.9 (C-3, 18), 127.2 (C-7), 133.0 (C-8), 139.4, 139.5 (C-4, 21), 143.2 (C-1, 20); δ_C (100 MHz, $CDCl_3$) 16.7 (C-9), 18.8 (C-14), 20.3 (C-6'), 24.8, 25.0 (C-5, 17), 27.5 (C-16), 28.4 (C-6), 29.2 (C-13), 37.4 (C-15), 42.2 (C-12), 45.2 (C-10), 67.9 (C-5'), 73.3 (C-11), 78.8, 79.2 (C-2', 3'), 90.5 (C-4'), 106.6 (C-1'), 111.0 (C-2, 19), 124.8, 125.1 (C-3, 18), 127.5 (C-7), 132.1 (C-8), 138.8, 138.9 (C-4, 21), 142.7 (C-1, 20); [Found (HRFABMS): MH^+, *m/z* 477.2874. $C_{27}H_{41}O_7$ requires 477.2852].

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