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The ^{13}C NMR Method for Determining the Absolute Configuration of the 1,2-Glycols Consisting of Secondary and Tertiary Hydroxyl Groups

Masaru Kobayashi*

Graduate School of Pharmaceutical Sciences, Hokkaido University, Kita-ku, Sapporo 060-0812, Japan

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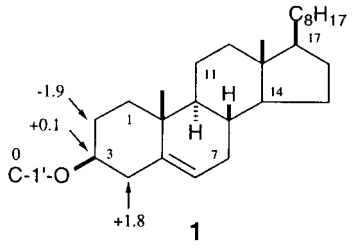
Abstract—The fucofuranoside method, the ^{13}C NMR method for determining the absolute configuration of secondary alcohols, is applied to five known steroids having a 1,2-glycol group composed of secondary and tertiary hydroxyl groups. The 1,2-alignment of the polar fucofuranosyl and tertiary hydroxyl group was found to have little influence on the requisite conformation of the glycosidic linkage. It showed the normal pattern of the distribution of the $\Delta\delta_C$ (and $\Delta\delta_H$) values, as previously observed for simple monohydroxy derivatives, demonstrating the usefulness of the method for this type of compound.

Introduction

The fucofuranoside method determines the absolute configuration of the secondary hydroxyl groups by converting to β-d- and β-l-fucofuranosides.[1] In the ^{1}H NMR it utilizes the uneven paramagnetic effect (pyridine-induced shift)[2] caused by the solvent pyridine molecules associated to the polar and chiral sugar moiety and derives the difference of the chemical shifts ($\Delta\delta_H=\delta_H^l-\delta_H^d$) of the two diastereomers. The principle of the method is, therefore, different from that of the Mosher ester[3–8] and other related methods[9–16] which utilize the anisotropy directly sent forth from the aromatic ester substituents. In every method, however, the requisite condition is that the essential substituent should take a pertinent conformation. The Mosher-type esters are generally composed of a few rotamers in equilibrium,[17–19] but the recognition of this is difficult unless based on complex molecular mechanic calculation. In contrast, the glycosidic linkages are subjected to the characteristic orientation (*exo*-anomeric) effect of the sugar moiety.[20,21] This could be recognized simply by the prominent NOEs observed between the proximate anomeric and the oxymethine (α-) protons.

However, such advantages of the fucofuranoside method in ^{1}H NMR are rather insignificant when compared with the by far more important fact that it enables the use of ^{13}C NMR for the same purpose.[1] As long as we rely on ^{1}H NMR spectroscopy, the derivation of the exact $\Delta\delta_H$ values for numerous proton signals using 2D spectra is time-consuming and avoidance of errors is often difficult.

The $\Delta\delta_C$ values ($\delta_C^l-\delta_C^d$) in the ^{13}C NMR derived from the β-d- and β-l-fucofuranosides originate from the difference in their glycosidation shifts.[22–24] This glycosidation shift depends on two factors: (A) The deshielding effect of the 4′-oxygen atom of the furanose unit when it nears one of the β-carbons of the aglycon (δ-effect).[25,26] (B) The deshielding contribution to each carbon atom (in this case the anomeric carbon C-1′ and α-carbon) of the two C–H bonds when they near 1,3-*syn*-periplanar alignment (HC interaction).[27–29] Accordingly, in contrast to the ^{1}H NMR methods, the necessary $\Delta\delta_C$ values are only four, those of the anomeric carbon, α-carbon, and two β-carbons. Typical examples (in ppm) are shown below.[1]



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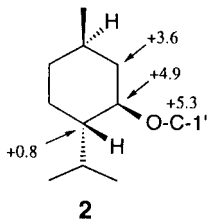

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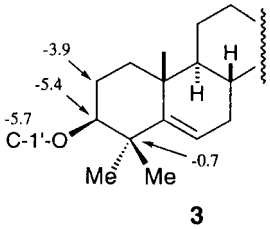

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The glycoside is viewed by fixing the α-proton below and the sugar moiety in front. If the two β-carbons bear

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* Fax: +81-011-706-4989; e-mail: masark@pharm.hokudai.ac.jp

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symmetrical steric hindrance, as in cholesterol (**1**), the factor B cancels out each other so that the $\Delta\delta_C$ value of the right β-carbon is positive but that of the left β-carbon is negative while the anomeric and α-carbon show negligible $\Delta\delta_C$ values. The principle is applicable to the cyclic tertiary alcohols substituted with methyl and two methylene groups.[30] When the steric hindrance is unsymmetrical, the $\Delta\delta_C$ values are defined by the order of (a) fucofuranosyl group (b) sterically bulkier β-position (c) less bulky β-position. If it is clockwise (R-type), as in *l*-menthol (**2**), the $\Delta\delta_C$ values of the anomeric, α-, and the right β-carbon are all large positive values while that of the left β-carbon is small (usually positive). In the counterclockwise (S-type) case, as in 4,4-dimethylcholesterol (**3**), the opposite results are obtained. In such cases, due to the distortion of the glycosidic linkage, the deshielding effect of both the factors A and B increases in one diastereomer, but decreases in the other diastereomer.[1] These $\Delta\delta_C$ values are therefore available in the spectra taken in the solvents other than pyridine-d_5.

Previous applications of the fucofuranoside method have been limited to the most simple compounds having a single hydroxyl group. It is necessary to extend the method to more complex compounds to prove its general applicability. There are many natural products having a 1,2-glycol group which is composed of one secondary and one tertiary hydroxyl groups. In such compounds it is possible to glycosidate the secondary hydroxyl group, leaving the tertiary one intact. If the interaction of both the strongly polar fucofuranosyl and the neighboring tertiary hydroxyl groups results in inappropriate glycosidic linkage conformation, this method would not be applicable. To examine this, we tried the fucofuranoside method for five such steroidal 1,2-glycols (**4**–**8**)[31] in pyridine-d_5.

The arrangement of the secondary hydroxyl groups is either axial (**4**, **6**) or equatorial (**5**, **7**, **8**), and the glycols are *cis* (**5**, **7**, **8**) or *trans* (**4**, **6**). These glycols were converted to monofucofuranosides using a previously reported procedure with fucofuranose tetraacetate, TMSOTf and 4A molecular sieve, followed by methanolysis (NaOMe in MeOH).[1] Under these conditions, the glycosides formed are predominantly β-anomer, as confirmed by the characteristic small coupling constant (less than 2.0 Hz) of the anomeric proton.[32] According to the above-mentioned conventional rule, the compounds **4** and **5** belong to the R-type while the compounds **6**, **7**, and **8** belong to the S-type compound.

The rough conformation of the glycosidic linkage is discernible from the NOE observed between the α- and anomeric protons. In the R-type glycosides, in contrast to the symmetrical cases, due to the distortion of the glycosidic linkage these two protons become closer in the l-isomer but become further detached in the d-isomer. In the S-type glycosides, this phenomenon occurs in the opposite way.[1] The NOE experiment of compounds **4** to **8** confirmed this. In the R-type compounds, the NOE is more significant in the l-isomer (**4**, 11%; **5**, 11%) than in the d-isomer (**4**, 5.4%; **5**, 6%). In contrast, in the S-type compound, the NOE is more significant in the d-isomer (**6**, 11%; **7**, 10%; **8**, 10%) than in the l-isomer (**6**, 4.7%; **7**, 6%; **8**, 2%). These results show that the pertinent conformation is indeed retained in the glycosidic linkage of the secondary hydroxyl group of such 1,2-glycols even when the hydroxyl group is axially oriented.

^{13}C NMR

The results of the ^{13}C NMR experiment are shown in Fig. 1. In the R-type compounds **4** and **5**, the $\Delta\delta_C$ of the anomeric, α- and the right β-carbon (**4**, C-7; **5**, C-3) are indeed large positive values while that of the left β-carbon (C-5) is a quite small positive value. In contrast, in the S-type compounds, the $\Delta\delta_C$ of the anomeric, α- and the left β-carbon (**6** and **8**, C-3; **7**, C-7) are large negative values while that of the right β-carbon (C-5) is a small negative value. Their magnitudes are almost the same when compared with those of the monohydroxy compounds **2** and **3**. By inversion of the configuration of the secondary hydroxyl group, the sign of the four $\Delta\delta_C$ values is changed in **4** and **7**, and in **5** and **6**. The A/B-*cis* steroid **8** shows the identical pattern of the $\Delta\delta_C$ values with those of the A/B-*trans* steroids **6** and **7**. Compounds **4** and **6**, and also the compounds **5** and **7** are antipodal, with respect to A- and B-rings, if we disregard the C-8 and C-9. These pairs show quite symmetrical $\Delta\delta_C$ values. We estimate the deviation of the chemical shifts, due to the small differences in concentration, temperature, or impurities in the solvent, to be less than 0.2 ppm. In other words, the ^{13}C NMR method is

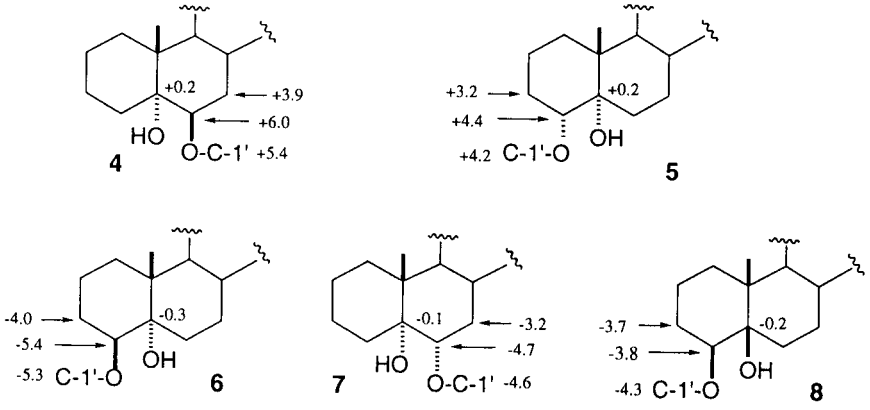

Figure 1. $\Delta\delta_C$ values (ppm).

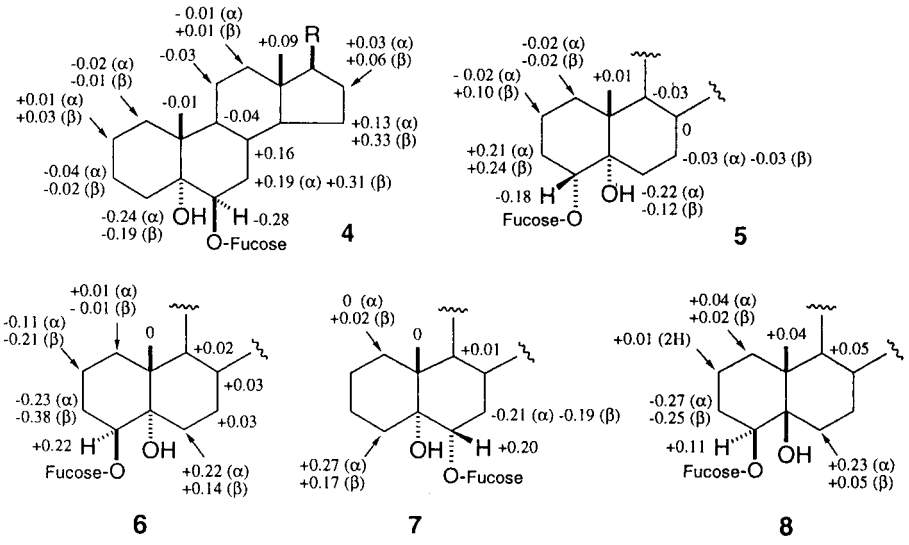

Figure 2. $\Delta\delta_H$ values (ppm).

impractical for determining the absolute configuration of secondary hydroxyl groups when the magnitude of its $\Delta\delta_C$ values is less than 0.2 ppm. The $\Delta\delta_C$ values obtained in the present study sufficiently exceed such experimental errors. The results indicate that the neighboring polar tertiary hydroxyl group hardly influences the requisite conformation of the glycosidic linkage. It simply contributes to the steric hindrance at the β-carbon. The results thus obtained are irrespective of the axial or equatorial, or *cis* or *trans* orientation of the hydroxyl groups. The advantage of the present method using ^{13}C NMR is that its principle is simple and that the result is easy to recognize compared with those of the various ^1H NMR methods (e.g. Fig. 2). The dominant cause of the difference of the chemical shift of the anomeric carbon, α-carbon, and two β-carbons, between the two diastereomeric fucofuranosides, is the above-mentioned δ-effect and the HC-interaction. Theoretically, therefore, the present method is applicable not only for such 1,2-glycols but also for other types of secondary alcohols, provided that they can be converted to fucofuranoside and the requisite conformation is confirmed by sufficient NOE intensity.

^{1}H NMR

In both the R-type and S-type compounds, the significant positive $\Delta\delta_H$ values are observed in the nearby right segment protons, while the negative values are observed in the left segment protons (Fig. 2). In accordance with the rule previously reported,[1] the $\Delta\delta_H$ value of the α-proton of the R-type compounds **4** and **5** is negative while that of the S-type compounds **6**, **7** and **8** is positive. Unlike the conformationally unstable aromatic ester methods, definite distributions of the $\Delta\delta_H$ values are observed for the axial hydroxyl groups (**4** and **6**). As can be seen in Fig. 2, however, the distribution of the $\Delta\delta_H$ values is rather complex and confusing when compared with the simple $\Delta\delta_C$ values shown in Fig. 1. Also, their magnitudes are arbitrary depending on the spatial arrangement of each proton relative to the polar fucofuranosyl group. The 2-H_2 of **6**, for example, is strongly influenced by the axial 4β-fucofuranosyl group but that of **8** is little influenced by the equatorial 4β-fucofuranosyl group. Some protons, such as 15-H_2 of **4**, are strongly influenced by the pyridine-induced shift of the remote fucofuranosyl group. It should be emphasized here, however, that the small $\Delta\delta_H$ values, less than 0.03 ppm, are less meaningful. The β-d- and β-l-fucofuranoside are diastereomeric so that even a slight difference due to the distortion of the aglycon framework can cause small changes in the chemical shifts which are unrelated to the pyridine-induced shifts. The ^1H NMR is of secondary importance in the fucofuranoside method, though the $\Delta\delta_H$ values obtained afford supplementary evidence for the absolute configuration.

Experimental

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 in pyridine-d_5 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. FAB mass spectra were determined on a JEOL JMS HX 110 mass spectrometer. Flash column chromatography was performed on silica gel (Wako gel C-300, 200–300 mesh, Wako Pure Chemical Industries).

Preparation of β-d- and β-l-fucofuranosides. A mixture of the alcohol (0.05 mmol), fucofuranose tetraacetate (0.1 mmol) and freshly dried 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. The mixture was diluted with $CHCl_3$, filtered, and the filtrate was evaporated to dryness. It was dissolved in 1 ml 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 eluting with 2–4% MeOH in $CHCl_3$ to give the β-fucofuranoside. The yields were 40–60% except for 6 which gave low yield of the product **6a** (17%) and **6b** (19%).

Cholestane-5α, 6β-diol 6-*O*-β-d-fucofuranoside 4a. Colorless oil; $[\alpha]_D^{23}=-67°$ (c=3.28, pyridine); δ_H 2.15 (1H, m, 3α-H), 2.61(1H, td, J=13.5, 4.0 Hz, 4β-H), 4.10 (1H, br s, 6α-H), 2.02 (1H, br d, J=12.5 Hz, 12β-H), 1.80 (1H, m, 16α-H), 0.65 (3H, s, 18-H_3), 1.35 (3H, s, 19-H_3), 5.54 (1H, br s, 1′-H), 1.58 (3H, d, J=6.5 Hz, 6′-H) [1.98 (1α-H), 1.40 (1β-H), 1.51 (2α-H), 1.36 (2β-H), 1.54 (3β-H), 1.64 (4α-H), 1.94 (7-H_2), 1.86 (8β-H), 1.90 (9α-H), 1.60 (11-H_2), 1.18 (12α-H), 1.57 (15α-H), 0.94 (15β-H), 1.21 (16β-H) detected by HSQC spectrum]; δ_C 33.7 (C-1), 21.2 (C-2), 21.2 (C-3), 32.4 (C-4), 73.4 (C-5), 79.3 (C-6), 30.0 (C-7), 31.3 (C-8), 46.1 (C-9), 39.5 (C-10), 21.8 (C-11), 40.6 (C-12), 43.0 (C-13), 56.5/56.6 (C-14), 24.5 (C-15), 28.6 (C-16), 56.6/56.5 (C-17), 12.5 (C-18), 16.5 (C-19), 106.2 (C-1′), 84.5 (C-2′), 79.7 (C-3′), 88.4 (C-4′), 67.5 (C-5′), 20.6 (C-6′); [Found: MNa^+, m/z 573.4103. $C_{33}H_{58}O_6$ Na requires 573.4131].

Cholestane-5α, 6β-diol 6-*O*-β-l-fucofuranoside 4b. Colorless oil; $[\alpha]_D^{23}=+28°$ (c=3.54, pyridine); δ_H 2.42 (1H, td, J=12.5, 4.0 Hz, 4β-H), 3.82 (1H, br t, J=2.5 Hz, 6α-H), 2.13 (1H, td, J=12.5, 3.0 Hz, 7α-H), 2.25 (1H, dt, J=12.5, 2.5 Hz, 7β-H), 0.74 (3H, s, 18-H_3), 1.34 (3H, s, 19-H_3), 5.49 (1H, br s, 1′-H), 1.63 (3H, d, J=6.5 Hz, 6′-H) [1.96 (1α-H), 1.39 (1β-H), 1.52 (2α-H), 1.39 (2β-H), 2.11 (3α-H), 1.52 (3β-H), 1.40 (4α-H), 2.02 (8β-H), 1.86 (9α-H), 1.57 (11-H_2), 1.17 (12α-H), 2.03 (12β-H), 1.70 (15α-H), 1.27(15β-H), 1.83 (16α-H), 1.27 (16β-H) detected by HSQC spectrum]; δ_C 33.7 (C-1), 21.3 (C-2), 21.1 (C-3), 32.2 (C-4), 73.6 (C-5), 85.3 (C-6), 33.9 (C-7), 31.5 (C-8), 46.0 (C-9), 39.6 (C-10), 21.7 (C-11), 40.7 (C-12), 43.1 (C-13), 56.7 (C-14), 24.5 (C-15), 28.6 (C-16), 56.7 (C-17), 12.5 (C-18), 16.8 (C-19), 111.6 (C-1′), 84.3 (C-2′), 79.2 (C-3′), 88.0 (C-4′), 67.2 (C-5′), 20.7 (C-6′); [Found: MNa^+, m/z 573.4105. $C_{33}H_{58}O_6$ Na requires 573.4131].

Cholestane-4α, 5α-diol 4-*O*-β-d-fucofuranoside 5a. Mp 178–180°C (from acetone); $[\alpha]_D^{23}=-20°$ (c=1.62, pyridine); δ_H 2.06 (1H, m, 3α-H), 4.07 (1H, dd, J=11.5, 5.0 Hz, 4β-H), 2.39 (1H, br d, J=12.7 Hz, 6α-H), 1.99 (1H, br dt, J=12.0, 3.0 Hz, 12β-H), 0.70 (3H, s, 18-H_3), 0.92 (3H, s, 19-H_3), 5.61 (1H, br s, 1′-H), 1.67 (3H, d, J=6.5 Hz, 6′-H) [1.82 (1α-H), 1.26 (1β-H), 1.57 (2α-H), 1.45 (2β-H), 1.93 (3β-H), 1.68 (6β-H), 1.63 (7α-H), 1.47 (7β-H), 1.40 (8β-H), 1.91 (9α-H) detected by HSQC spectrum]; δ_C 31.1 (C-1), 20.2 (C-2), 26.0 (C-3), 75.8 (C-4), 74.7 (C-5), 29.7 (C-6), 26.7 (C-7), 35.0 (C-8), 45.7 (C-9), 41.1 (C-10), 21.4 (C-11), 40.6 (C-12), 42.9 (C-13), 56.6/56.7 (C-14), 24.5 (C-15), 28.6 (C-16), 56.7/56.6 (C-17), 12.4 (C-18), 15.6 (C-19), 106.6 (C-1′), 84.4 (C-2′), 79.6 (C-3′), 88.4 (C-4′), 67.7 (C-5′), 20.5 (C-6′); [Found: MNa^+, m/z 573.4115. $C_{33}H_{58}O_6$ Na requires 573.4131].

Cholestane-4α, 5α-diol 4-*O*-β-l-fucofuranoside 5b. Colorless oil; $[\alpha]_D^{23}=+60°$ (c=2.18, pyridine); δ_H 1.80 (1H, td, J=12.5, 5.5 Hz, 1α-H), 2.27 (1H, qd, J=11.5, 5.5 Hz, 3α-H), 2.17 (1H, m, 3β-H), 3.89 (1H, dd, J=11.5, 5.5 Hz, 4β-H), 2.17 (1H, m, 6α-H), 1.99 (1H, br dt, J=12.0, 3.0 Hz, 12β-H), 0.69 (3H, s, 18-H_3), 0.93 (3H, s, 19-H_3), 5.56 (1H, d, J=1.5 Hz, 1′-H), 1.63(3H, d, J=6.5 Hz, 6′-H) [1.24 (1β-H), 1.55 (2-H_2), 1.56 (6β-H), 1.60 (7α-H), 1.44 (7β-H), 1.40 (8β-H), 1.88 (9α-H) detected by HSQC spectrum]; δ_C 31.0 (C-1), 20.4 (C-2), 29.2 (C-3), 80.2 (C-4), 74.9 (C-5), 29.4 (C-6), 26.6 (C-7), 35.0 (C-8), 45.7 (C-9), 40.9 (C-10), 21.3 (C-11), 40.6 (C-12), 42.8 (C-13), 56.6 (C-14), 24.4 (C-15), 28.6 (C-16), 56.6 (C-17), 12.4 (C-18), 15.5 (C-19), 110.8 (C-1′), 83.8 (C-2′), 79.5 (C-3′), 88.4 (C-4′), 67.7 (C-5′), 20.5 (C-6′); [Found: MNa^+, m/z 573.4114. $C_{33}H_{58}O_6$ Na requires 573.4131].

Cholestane-4β, 5α-diol 4-*O*-β-d-fucofuranoside 6a. Mp 173–175°C (from acetone); $[\alpha]_D^{23}=+1.7°$ (c=1.76, pyridine); δ_H 2.11 (1H, qt, J=12.5, 3.5 Hz, 2β-H), 2.50 (1H, tt, J=13.0, 4.0 Hz, 3α-H), 2.19 (1H, br d, J=13.0 Hz, 3β-H), 3.87 (1H, br s, 4α-H), 2.36 (1H, td, J=13.0, 4.5 Hz, 6β-H), 1.73 (1H, qd, J=12.5, 4.0 Hz, 7α-H), 2.01 (1H, br d, J=12.0 Hz, 12β-H), 0.71 (3H, s, 18-H_3), 1.33 (3H, s, 19-H_3), 5.52 (1H, d, J=2.0 Hz, 1′-H), 1.61 (3H, d, J=6.5 Hz, 6′-H) [1.89 (1α-H), 1.42 (1β-H), 1.56 (2α-H), 1.42 (6α-H), 1.48 (7β-H), 1.44 (8β-H), 1.90 (9α-H), detected by HSQC spectrum]; δ_C 32.2 (C-1), 18.2 (C-2), 28.1 (C-3), 84.9 (C-4), 73.7 (C-5), 32.0 (C-6), 26.6 (C-7), 35.2 (C-8), 46.8 (C-9), 39.5 (C-10), 20.7 (C-11), 40.6 (C-12), 43.0 (C-13), 56.6/56.7 (C-14), 24.5 (C-15), 28.6 (C-16), 56.7/56.6 (C-17), 12.4 (C-18), 15.8 (C-19), 111.6 (C-1′), 84.5 (C-2′), 79.3 (C-3′), 88.1 (C-4′), 67.6 (C-5′), 20.5 (C-6′); [Found: MNa^+, m/z 573.4135. $C_{33}H_{58}O_6$ Na requires 573.4131].

Cholestane-4β, 5α-diol 4-*O*-β-l-fucofuranoside 6b. Colorless oil; $[\alpha]_D^{23}=+75°$ (c=1.96, pyridine); δ_H 2.27 (1H, br tt, J=12.0, 4.0 Hz, 3α-H), 4.09 (1H, br s, 4α-H), 2.50 (1H, td, J=13.5, 4.5 Hz, 6β-H), 2.02 (1H, br d, J=12.5 Hz, 12β-H), 0.72 (3H, s, 18-H_3), 1.33 (3H, s, 19-H_3), 5.48 (1H, br s, 1′-H), 1.60 (3H, d, J=6.5 Hz, 6′-H) [1.90 (1α-H), 1.41 (1β-H), 1.45 (2α-H), 1.90 (2β-H), 1.81 (3β-H), 1.64 (6α-H), 1.76 (7α-H), 1.51 (7β-H), 1.48 (8β-H), 1.92 (9α-H) detected by HSQC spectrum]; δ_C 32.4 (C-1), 17.8 (C-2), 24.1 (C-3), 79.5 (C-4), 73.4 (C-5), 32.2 (C-6), 26.6 (C-7), 35.3 (C-8), 46.9 (C-9), 39.5 (C-10), 20.8 (C-11), 40.7 (C-12), 43.1 (C-13), 56.7/56.8 (C-14), 24.5 (C-15), 28.6 (C-16), 56.8/56.7 (C-17), 12.5 (C-18), 15.8 (C-19), 106.3 (C-1′), 84.7 (C-2′), 79.8 (C-3′), 88.3 (C-4′), 67.5 (C-5′), 20.6 (C-6′); [Found: MNa^+, m/z 573.4123. $C_{33}H_{58}O_6$ Na requires 573.4131].

Cholestane-5α, 6α-diol 6-*O*-β-d-fucofuranoside 7a. Mp 183–186°C (from acetone); $[\alpha]_D^{23}=-33°$ (c=3.20, pyridine); δ_H 1.89 (1H, m, 1α-H), 2.12 (1H, m, 4α-H), 3.82 (1H, dd, J=11.0, 5.0 Hz, 6β-H), 2.14 (1H, m, 7α-H), 0.66 (3H, s, 18-H_3), 0.94 (3H, s, 19-H_3), 5.56 (1H, d, J=1.5 Hz, 1′-H), 1.63 (3H, d, J=6.5 Hz, 6′-H) [1.32 (1β-H), 1.54 (4β-H), 1.92 (7β-H), 1.81 (9α-H), 1.97 (12β-H) detected by HSQC spectrum]; δ_C 32.2 (C-1), 21.3/21.6 (C-2), 21.6/21.3 (C-3), 29.7 (C-4), 74.7 (C-5), 79.9 (C-6), 34.6 (C-7), 34.2 (C-8), 45.1 (C-9), 40.3 (C-10), 21.0 (C-11), 40.5 (C-12), 43.0 (C-13), 56.6 (C-14), 24.4 (C-15), 28.6 (C-16), 56.6 (C-17), 12.4 (C-18), 15.6 (C-19), 110.9 (C-1′), 83.9 (C-2′), 79.4

(C-3′), 88.2 (C-4′), 67.5 (C-5′), 20.6 (C-6′); [Found: MNa^+, *m*/*z* 573.4109. $C_{33}H_{58}O_6$ Na requires 573.4131].

Cholestane-5α, 6α-diol 6-*O*-β-l-fucofuranoside 7b. Colorless oil; $[\alpha]_D^{23}=+61°$ (*c*=3.00, pyridine); δ_H 2.39 (1H, br d, *J*=13.5 Hz, 4α-H), 4.02 (1H, dd, *J*=12.0, 5.0 Hz, 6β-H), 0.68 (3H, s, 18-H_3), 0.94 (3H, s, 19-H_3), 5.66 (1H, d, *J*=1.5 Hz, 1′-H), 1.65 (3H, d, *J*=6.5 Hz, 6′-H) [1.89 (1α-H), 1.34 (1β-H), 1.71 (4β-H), 1.95 (7α-H), 1.72 (7β-H), 1.82 (9α-H), 1.98 (12β-H) detected by HSQC spectrum]; δ_C 32.3 (C-1), 21.3/21.6 (C-2), 21.6/21.3 (C-3), 30.0 (C-4), 74.6 (C-5), 75.2 (C-6), 31.4 (C-7), 34.1 (C-8), 45.3 (C-9), 40.5 (C-10), 21.2 (C-11), 40.4 (C-12), 43.0 (C-13), 56.6 (C-14), 24.4 (C-15), 28.5 (C-16), 56.6 (C-17), 12.4 (C-18), 15.7 (C-19), 106.3 (C-1′), 84.4 (C-2′), 79.5 (C-3′), 88.4 (C-4′), 67.7 (C-5′), 20.5 (C-6′); [Found: MNa^+, *m*/*z* 573.4123. $C_{33}H_{58}O_6$ Na requires 573.4131].

Cholestane-4β, 5β-diol 4-*O*-β-d-fucofuranoside 8a. Mp 97–102°C (from acetone); $[\alpha]_D^{23}=-21°$ (*c*=4.52, pyridine); δ_H 1.86 (1H, m, 1β-H), 2.29 (1H, m, 3α-H), 2.21 (1H, m, 3β-H), 4.36 (1H, dd, *J*=11.0, 5.5 Hz, 4α-H), 2.29 (1H, m, 6α-H), 1.74 (1H, td, *J*=13.5, 4.0 Hz, 6β-H), 1.97 (1H, br d, *J*=12.5 Hz, 12β-H), 0.67 (3H, s, 18-H_3), 1.17 (3H, s, 19-H_3), 5.65 (1H, d, *J*=1.5 Hz, 1′-H), 1.62 (3H, d, *J*=6.5 Hz, 6′-H) [1.43 (1α-H), 1.44 (2-H_2), 1.30 (9α-H), detected by HSQC spectrum]; δ_C 31.0 (C-1), 19.5 (C-2), 29.9 (C-3), 76.3 (C-4), 75.3 (C-5), 30.5 (C-6), 28.8 (C-7), 35.2 (C-8), 43.3 (C-9), 42.0 (C-10), 21.3 (C-11), 40.2 (C-12), 42.8 (C-13), 56.5/56.6 (C-14), 24.4 (C-15), 28.6 (C-16), 56.6/56.5 (C-17), 12.3 (C-18), 17.7 (C-19), 110.7 (C-1′), 83.8 (C-2′), 79.3 (C-3′), 88.4 (C-4′), 67.6 (C-5′), 20.6 (C-6′); [Found: MNa^+, *m*/*z* 573.4103. $C_{33}H_{58}O_6$ Na requires 573.4131].

Cholestane-4β, 5β-diol 4-*O*-β-l-fucofuranoside 8b. Colorless oil; $[\alpha]_D^{23}=+69°$ (*c*=3.68, pyridine); δ_H 1.88 (1H, td, *J*=13.5, 4.5 Hz, 1β-H), 2.52 (1H, br d, *J*=13.0 Hz, 6α-H), 1.79 (1H, td, *J*=13.0, 5.5 Hz, 6β-H), 0.68 (3H, s, 18-H_3), 1.21 (3H, s, 19-H_3), 5.65 (1H, s, 1′-H), 1.65 (3H, d, *J*=6.5 Hz, 6′-H) [1.47 (1α-H), 1.45 (2-H_2), 2.02 (3α-H), 1.96 (3β-H), 4.47 (4α-H), 1.35 (9α-H), 1.97 (12β-H) detected by HSQC spectrum]; δ_C 31.2 (C-1), 19.2 (C-2), 26.2 (C-3), 72.5 (C-4), 75.1 (C-5), 30.5 (C-6), 27.9 (C-7), 35.2 (C-8), 43.5 (C-9), 42.0 (C-10), 21.4 (C-11), 40.3 (C-12), 42.8 (C-13), 56.5/56.8 (C-14), 24.5 (C-15), 28.5 (C-16), 56.8/56.5 (C-17), 12.3 (C-18), 17.7 (C-19), 106.4 (C-1′), 84.1 (C-2′), 79.2 (C-3′), 88.3 (C-4′), 67.2 (C-5′), 20.7 (C-6′); [Found: MNa^+, *m*/*z* 573.4155. $C_{33}H_{58}O_6$ Na requires 573.4131].

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References

1. Kobayashi, M. *Tetrahedron* **1997**, *53*, 5973–5994.
2. Demarco, P. V.; Farkas, E.; Doddrell, D.; Mylari, B. L.; Wenkert, E. *J. Am. Chem. Soc.* **1968**, *90*, 5480–5486.
3. Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512–519.
4. Sullivan, G. R.; Dale, J. A.; Mosher, H. S. *J. Org. Chem.* **1973**, *38*, 2143–2147.
5. Kusumi, T.; Ohtani, I.; Inouye, Y.; Kakisawa, H. *Tetrahedron Lett.* **1988**, *29*, 4731–4734.
6. Ohtani, I.; Kusumi, T.; Ishitsuka, M. O.; Kakisawa, H. *Tetrahedron Lett.* **1989**, *30*, 3147–3147.
7. Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Org. Chem.* **1991**, *56*, 1296–1298.
8. Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092–4096.
9. Trost, B. M.; Curran, D. P. *Tetrahedron Lett.* **1981**, *22*, 4929–4932.
10. Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balcovec, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. P. *J. Org. Chem.* **1986**, *51*, 2370–2374.
11. Adamczeski, M.; Quinoa, E.; Crews, P. *J. Org. Chem.* **1990**, *55*, 240–242.
12. Kusumi, T.; Takahashi, H.; Xu, P.; Fukushima, T.; Asakawa, Y.; Hashimoto, T.; Kan, Y.; Inouye, Y. *Tetrahedron Lett.* **1994**, *35*, 4397–4400.
13. Seco, J. M.; Latypov, S.; Quinoa, E.; Riguera, R. *Tetrahedron Lett.* **1994**, *35*, 2921–2924.
14. Seco, J. M.; Latypov, S.; Quinoa, E.; Riguera, R. *Tetrahedron: Asymmetry* **1995**, *6*, 107–110.
15. Trujillo, M.; Morales, E. Q.; Vazquez, J. T. *J. Org. Chem.* **1994**, *59*, 6637–6642.
16. Fukushi, Y.; Yajima, C.; Mizutani, J. *Tetrahedron Lett.* **1994**, *35*, 599–602.
17. Latypov, S. K.; Seco, J. M.; Quinoa, E.; Riguera, R. *J. Org. Chem.* **1995**, *60*, 504–515.
18. Latypov, S. K.; Seco, J. M.; Quinoa, E.; Riguera, R. *J. Org. Chem.* **1996**, *61*, 8569–8577.
19. Latypov, S. K.; Seco, J. M.; Quinoa, E.; Riguera, R. *J. Am. Chem. Soc.* **1998**, *120*, 877–882.
20. Lemieux, R. U.; Pavia, A. A.; Martin, J. C.; Watanabe, K. A.; Can *J. Chem.* **1969**, *7*, 4427–4439.
21. Lemieux, R. U.; Koto, S. *Tetrahedron.* **1974**, *30*, 1933–1944.
22. Kasai, R.; Suzuo, M.; Asakawa, J.; Tanaka, O. *Tetrahedron Lett.* **1977**, 175–178.
23. Tori, K.; Seo, S.; Yoshimura, Y.; Arita, H.; Tomita, Y. *Tetrahedron Lett.* **1977**, 79–182.
24. Seo, S.; Tomita, Y.; Tori, K.; Yoshimura, Y. *J. Am. Chem. Soc.* **1978**, *100*, 3331–3339 Corrigenda, **1980**, *102*, 2512 and 7618.
25. Beierbeck, H.; Saunders, J. K.; Can *J. Chem.* **1976**, *54*, 2985–2995.
26. Eggert, H.; VanAntwerp, C. L.; Bhakka, N. S.; Djerassi, C. J. *Org. Chem.* **1976**, *41*, 71–78.
27. Beierbeck, H.; Saunders, J. K.; Can *J. Chem.* **1975**, *53*, 1307–1313.
28. Beierbeck, H.; Saunders, J. K.; ApSimon, J. W.; Can *J. Chem.* **1977**, *55*, 2813–2828.
29. Beierbeck, H.; Saunders, J. K. *Can. J. Chem.* **1980**, *58*, 1258–1265. In the lit.1, the ‘HC interaction’ was mistakenly described as HC gauche interaction.
30. Kobayashi, M. *Tetrahedron* **1998**, *54*, 10987–10998.
31. Coxon, J. M.; Gibson, J. R.; Aust *J. Chem.* **1981**, *34*, 1451–1465.
32. Prihar, H. S.; Tsai, J. H.; Wanamaker, S. R.; Duber, S. J.; Behrman, E. J. *Carbohydr. Res.* **1977**, *56*, 315–324.