Distinction of Absolute Configuration at C-22 of C-23-Hydroxyspirostane and C-23-Hydroxyspirosolane Glycosides

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It has been revealed that the absolute configurations at C-22 of 23-hydroxyspirostane and 23-hydroxyspirosolane could be unambiguouly judged by the ^{1}H- and ^{13}C-NMR spectroscopies.

Key words C-22 absolute configuration; 23-hydroxyspirostane; 23-hydroxyspirosolane

Naturally occurring usual spirostanes such as diosgenin and their glycosides are normally 22*R* configuration. On the other hand, spirosolanes such as tomatidine, solasodine and their glycosides take both 22*R* and 22*S* configurations (Chart 1). To determine the configuration at C-22 is very important, because the difference in C-22 configuration relates to the chemical reactions and bio-activity, for example, as shown in the following reaction of spirosolane derivatives. Esculeogenin A[1,2] with a 22*S* configuration isolated from ripe tomato fruits was easily converted to a pregnane derivative,[3] 3β,16β-dihydroxy-(5α)-pregn-20-one, by reaction with pyridine and water, while isoesculeogenin A[4] with a 22*R* configuration also obtained from tomato fruits, was transferred into esculeogenin B[2] by refluxing with pyridine and water (Chart 2).

Generally, it is very crucial for determing the configurations at C-22 of spirostane and spirosolane derivatives; however, it has become apparent that the C-23-hydroxyspirostane and hydroxyspirosolane derivatives are conventionally decided based on the ^{1}H- and ^{13}C-NMR spectroscopies. This paper describes how to decide their configuration at C-22.

In spirostane derivatives, the signals due to the H_3-21 and H-16 of 23*S*-hydroxydiosgenin[5] appeared at δ 1.18 (3H, d, J=6.7 Hz) and 4.64 (1H, dd, J=7.6, 15.6 Hz), respectively; on the other hand, those in (22*R*,23*S*,25*S*)-3β,6α,23-trihydroxy-(5α)-spirostane, torvogenin,[6] appeared at δ 1.52 (3H, d, J=7.3 Hz) and δ 5.22 (1H, dd, J=4.1, 13.2 Hz), respectively. The signal assigned to the H-16 in the 22*R* (22-β-*O*-)

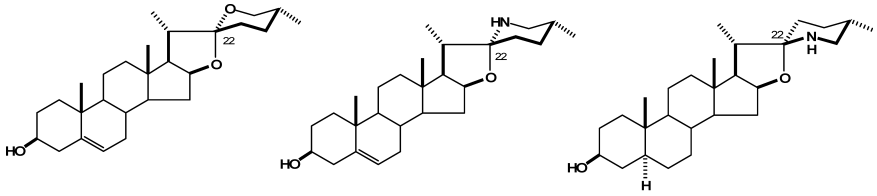

Chart 1

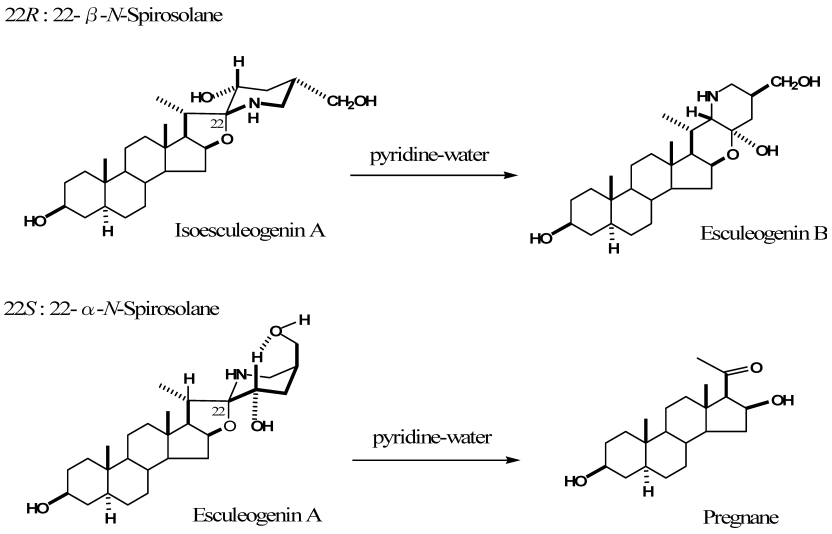

Chart 2

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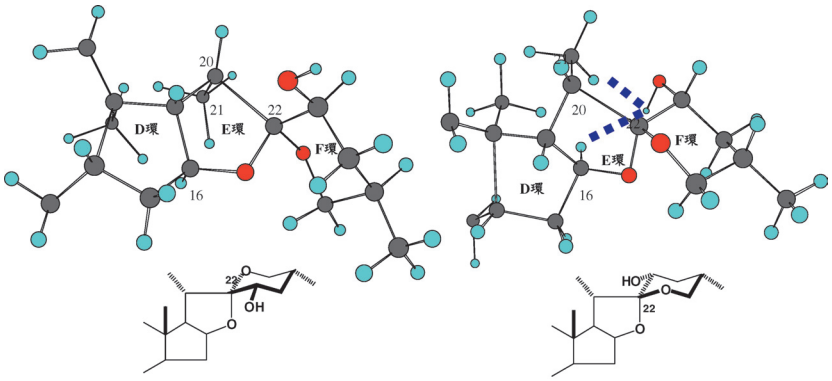
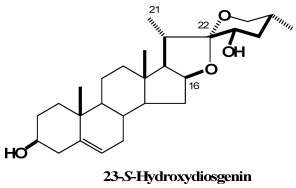
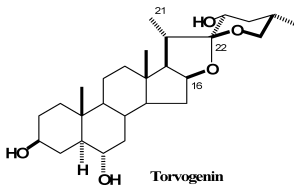


Fig. 1

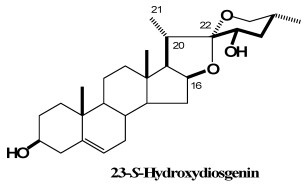
Table 1. Key ^{1}H-Chemical Shifts of 23*S*-Hydroxydiosgenin and Torvogenin

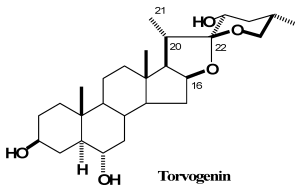




	22*S* (22-α-*O*-)		22*R* (22-β-*O*-)
H_3-21	δ 1.18 (d, *J*=6.7)	[Δ0.34 ppm]	δ 1.52 (d, *J*=7.3)
H-16	δ 4.64 (dd, *J*=7.6, 15.6)	[Δ0.58 ppm]	δ 5.22 (dd, *J*=4.1, 13.2)

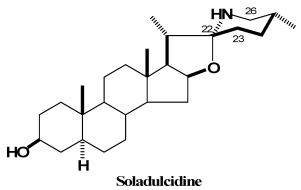
Table 2. Key ^{13}C-Chemical Shifts of 23*S*-Hydroxydiosgenin and Torvogenin

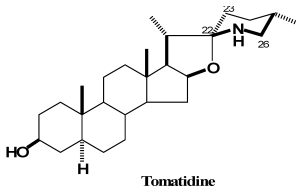




	22*S* (22-α-*O*-)		22*R* (22-β-*O*-)
C-16	δ 81.6	[Δ2.7 ppm]	δ 84.3
C-20	δ 35.8	[Δ7.2 ppm]	δ 43.0
C-21	δ 14.7	[Δ2.1 ppm]	δ 16.8

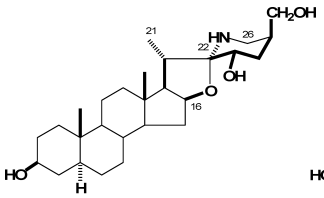
Table 3. Key ^{13}C-Chemical Shifts of Soladulcidine and Tomatidine

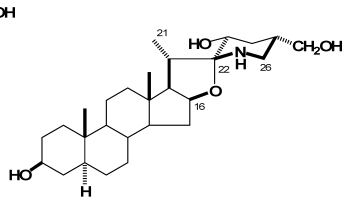




	22*R* (22-α-*N*-)		22*S* (22-β-*N*-)
C-23	δ 33.3	[Δ6.7 ppm]	δ 26.6
C-26	δ 46.9	[Δ3.3 ppm]	δ 50.2

Table 4. Key ^{1}H-Chemical Shifts of Esculeogenin A and Isoesculeogenin A





	22*S* (22-α-*N*-)		22*R* (22-β-*N*-)
H_3-21	δ 1.08 (d, *J*=6.7)	[Δ0.46 ppm]	δ 1.54 (d, *J*=6.8)
H-16	δ 4.49 (dd, *J*=7.3)	[Δ0.80 ppm]	δ 6.29 (m)

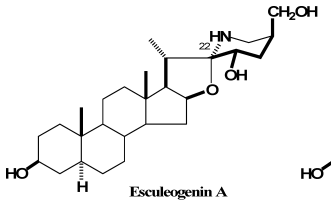
spirostanol sapogenol, is extremely lower—shifted by 0.58 ppm by comparing with that of the 22*S* (22-α-*O*-) spirostane sapogenol, 23*S*-hydroxydiosgenin. This is a probable reason that the hydroxyl group at C-23 in torvogenin with 22*R* (22-β-*O*-) orients to pyridine as solvent, whose anisotropic effect shifts the signals due to H_3-21 and H-16, toward lower field (Table 1), because H_3-21 and H-16 lie close to the hydroxyl group at C-23 (Fig 1).

Next, a comparative study of the ^{13}C-NMR spectra showed that the distinction of *R* or *S* could be dependent upon the chemical shift of the signal at C-20. That is, the signal due to the C-20 in the spirostanol in 23*S*-hydroxydiosgenin with 22*S* (22-α-*O*-) configuration appeared at δ 35.8, while the signal due to one of the C-22*R* (22-β-*O*-) occurred at δ 43.0 in torvogenin (Table 2).

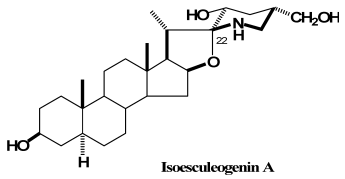
In the case of normal spirostane derivatives, 22*R*-configurations are predominant; however, in the case of spirosolane derivatives, two types of naturally occurring 22*R* and 22*S* are found such as soladulcidine (22*R*) and tomatidine (22*S*). Distinction of the C-22 configuration in soladulcidine and tomatidine could be attained by the chemical shifts at C-23 and C-26 as listed in Table 3. In the soladulcidine (22*R*:-22-α-*N*-) case, the signals due to C-23 and C-26 appeared at δ 33.3 and 46.9, respectively, while, in tomatidine (22*S*:22-β-*N*-), they occurred at δ 26.6 and 50.2, respectively (Table 3).

Recently, we have isolated novel tomato steroidal alkaloid glycosides, esculeosides A,[1,2] B, and lycoperoside F.[7] Esculeogenin A and isoesculeogenin A were obtaind by acid hydrolysis of esculeoside A and lycoperoside F, respectively.

Table 5. Key ^{13}C-Chemical Shifts of Esculeogenin A and Isoesculeogenin A



Esculeogenin A



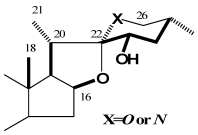
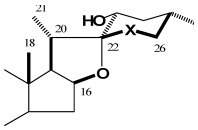
Isoesculeogenin A

	22*S* (22-α-*N*-)		22*R* (22-β-*N*-)
C-20	δ 35.0	[Δ9.1 ppm]	δ 44.1

The ^{1}H-NMR spectrum of esculeogenin A (22*S*:22-α-*N*-) showed signals due to H_3-21 at δ 1.08 (3H, d, J=6.7 Hz) and H-16 at δ 4.49 (1H, dd, J=7.3 Hz). Their ^{1}H signals of isoesculeogenin A appeared at δ 1.54 (3H, d, J=6.8 Hz, H_3-21) and 5.29 (1H, m, H-16) as listed in Table 4. These chemical shifts are coincident with those of 23-hydroxyspirostane derivatives in Table 4. The ^{13}C-NMR signals at C-20 exhibited respective chemical shift at δ 35.0 and 44.1 in esculeogenin A and isoesculeogenin A as listed in Table 5.

Consequently, in the 23-hydroxyspirostane and 23-hydroxyspirosolane, the ^{1}H- and ^{13}C-NMR chemical shifts of the signals due to H_3-21, H-16 and C-20 provided novel information for distinction of the configuration at C-22 as listed in Table 6. Therefore, to determine the configuration at C-22 is of course crucial.

Table 6. Discrimination by Key ^{1}H- and ^{13}C-Chemical Shift of 23-Hydroxyspirostane and 23-Hydroxyshirosolane

	H_3-21	H-16	C-20
 X=*O* or *N*	δ=1.08—1.26	4.49—4.56	35.0—36.2
	δ=1.52—1.54	5.18—5.29	43.0—44.1

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