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-hydroxy-spirosolane could be unambiguously judged by the 1H- and 13C-NMR spectroscopies.

Key words C-22 absolute configuration; 23-hydroxyspirostane; 23-hydroxy-spirosolane

Naturally occurring usual spirostanes such as diosgenin and their glycosides are normally 22R configuration. On the other hand, spirosolanes such as tomatidine, solasodine and their glycosides take both 22R and 22S 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 A1,2) with a 22S 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 A4) with a 22R configuration also obtained from tomato fruits, was transferred into esculeogenin B2) by refluxing with pyridine and water (Chart 2).

Generally, it is very crucial for determining 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 1H- and 13C-NMR spectroscopies. This paper describes how to decide their configuration at C-22.

In spirostane derivatives, the signals due to the H-21 and H-16 of 23S-hydroxydiosgenin5) 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 (22R,23S,25S)-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 22R (22-β-O-)

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spirostanol sapogenol, is extremely lower—shifted by 0.58 ppm by comparing with that of the 22S (22α-O-)
spirostane sapogenol, 23S-hydroxydiosgenin. This is a probable reason that the hydroxyl group at C-23 in torvogenin with
22R (22β-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 13C-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 23S-hydroxydiosgenin with
22S (22α-O-) configuration appeared at δ 35.8, while the
signal due to one of the C-22R (22β-O-) occurred at δ 43.0
in torvogenin (Table 2).

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

Recently, we have isolated novel tomato steroidal alkaloid
glycosides, esculeosides A, B, and lycoperoside F.7) Es-
culeogenin A and isoeesculeogenin A were obtained by acid
hydrolysis of esculeoside A and lycoperoside F, respectively.
The $^1$H-NMR spectrum of esculeogenin A (22S,22-α-N-) showed signals due to H$_{3}$-21 at $\delta$ 1.08 (3H, d, $J$ = 6.7 Hz) and H-16 at $\delta$ 4.49 (1H, dd, $J$ = 7.3 Hz). Their $^1$H signals of isoesculeogenin A appeared at $\delta$ 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 $\delta$ 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 5. Key $^{13}$C-Chemical Shifts of Esculeogenin A and Isoesculeogenin A

<table>
<thead>
<tr>
<th></th>
<th>$\delta$ 35.0</th>
<th>[49.1 ppm]</th>
<th>$\delta$ 44.1</th>
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<tr>
<td>C-20</td>
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<tr>
<td>22S (22-α-N-)</td>
<td>35.0</td>
<td>[49.1 ppm]</td>
<td>44.1</td>
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<tr>
<td>22R (22-β-N-)</td>
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### Table 6. Discrimination by Key $^1$H- and $^{13}$C-Chemical Shift of 23-Hydroxyspirostane and 23-Hydroxyspirosolane

<table>
<thead>
<tr>
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<th>H$_{3}$-21</th>
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<th>C-20</th>
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<tbody>
<tr>
<td>H$_{3}$-21</td>
<td>$\delta$ 1.08—1.26</td>
<td>4.49—4.56</td>
<td>35.0—36.2</td>
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<tr>
<td>H-16</td>
<td>$\delta$ 1.52—1.54</td>
<td>5.18—5.29</td>
<td>43.0—44.1</td>
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### References