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Conversion of Furostanol Glycosides into Steroidal Alkaloid Glycosides. I. From Methyl Protodioscin to Kryptogenin 3-*O*-*β*-Chacotrioside

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A furostanol glycoside, methyl protodioscin (**1**), was converted to kryptogenin 3-*O*-*β*-chacotrioside (**4**), which is a key intermediate in the chemical transformation to the solanidane glycoside.

Keywords——chemical conversion; furostanol glycoside; methyl protodioscin; kryptogenin glycoside; chacotrioside; steroidal alkaloid glycoside; oxidation

Kryptogenin (**5**) is regarded as a key intermediate in the course of transformation from steroidal sapogenols to the bioactive steroidal alkaloids, 22, 25-isosolanidine or solasodine.[2)] We have now succeeded in the transformation of a furostanol glycoside, methyl protodioscin (**1**),[3)] into kryptogenin 3-*O*-*β*-chacotrioside (**4**), as the first step in an attempt to obtain the solanidane glycoside.

Methyl protodioscin (**1**), obtained from *Trillium tschonoskii* in *ca.* 2.3% yield, was acetylated with Ac_2O–pyridine and the resultant acetate was then oxidized with the Jones reagent (a mixture of CrO_3 and H_2SO_4 in dil. acetone), followed by saponification with 3% KOH–MeOH to give a mixture of two predominent compounds. They were separated by silica gel column chromatography (eluted with $CHCl_3$–MeOH–H_2O (7:3:0.2)) to give a major oxidative product **2** (yield, 69%) and a by-product **3** (25%). Compound **2** was recrystallized from dil. MeOH to give colorless needles, mp 204—207 °C, which showed a peak at *m/z* 1069.0 arising from $[M+Na]^+$ in fast atom bombardment mass spectrometry (FAB-MS), absorptions due to the carbonyl groups at 1735 and 1710 cm^{-1} and a strong band due to hydroxyl groups at 3400 cm^{-1} in the infrared (IR) spectrum. Its circular dichroism (CD) spectrum exhibited a negative Cotton effect ($[\theta]: -1.64\times10^4$) at 294 nm, and was consistent with that of kryptogenin. Compound **3**, colorless needles, mp 268—271 °C, FAB-MS (*m/z*): 807.8 $[M+K]^+$, 791.6 $[M+Na]^+$, was identified as 3-*O*-*β*-chacotriosyl pregn-5, 16-dien-20-one[4)] on the basis of the carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum and direct comparison with an authentic specimen. Compound **2** was subsequently hydrolyzed with *β*-glucosidase to furnish a product **4** (yield 80% from **2**), which was recrystallized from dil. MeOH to give colorless needles, mp 231—234 °C, CD $[\theta]$nm: -1.79×10^4 (294) (negative Cotton), IR ν_{max}^{KBr} cm^{-1}: 3400, 1735, 1710. Compound **4** showed peaks at *m/z* 923.6 and 907.9 originating from $[M+K]^+$ and $[M+Na]^+$ in the FAB-MS. The ^{13}C-NMR spectrum showed a total of forty-five carbon signals, which indicated that the aglycone part (except C-2 to C-4) resembled those of kryptogenin,[5)] while the sugar signals were superimposable on those of the *β*-chacotriosyl residue[6)] of methyl protodioscin (Table I).

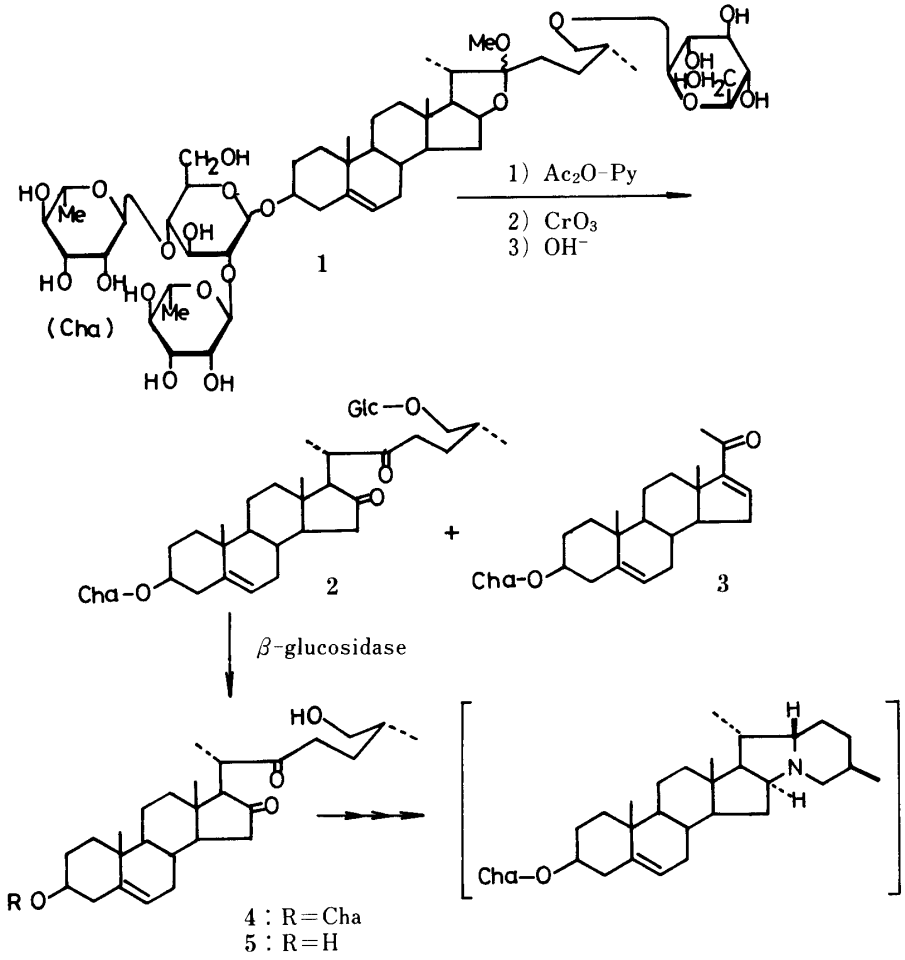

Chart 1

The above spectral data suggested **4** to be kryptogenin 3-*O*-*β*-chacotrioside. Compound **4** was eventually obtained from **1** in 55% yield. This is the first example of conversion of a furostanol glycoside to a kryptogenin glycoside. This new oxidative reaction provides a simple route to the kryptogenin glycosides in good yield. We are investigating a route *via* the 16-benzyloxime to convert **4** into pharmacologically active steroidal alkaloid glycosides.

Experimental

All melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. IR spectra were recorded on a JASCO DS-701 G spectrometer and ^{13}C-NMR spectra were taken on a JEOL FX-200 spectrometer with tetramethylsilane as an internal standard. MS were recorded with a JEOL JMS-01SG instrument. CD spectra were recorded with a JASCO J-50A spectrometer.

3-*O*-*β*-Chacotriosyl Kryptogenin 26-*O*-*β*-D-Glucoside (2)——A solution of methyl protodioscin (**1**), 3.17 g, in pyridine (25 ml) and anhydrous acetic acid (12 ml) was heated on a hot bath for 1 h, and the reaction mixture was worked-up in the usual way to provide the acetate, which was then dissolved in acetone (50 ml) and oxidized with Jones reagent (monitored by thin layer chromatography (TLC) using Ehrlich reagent[7] as the spraying agent). The oxidative product was dissolved in MeOH (20 ml), saponified by treatment with 3% KOH–MeOH (20 ml) for 1 h at room temperature and neutralized with 1 N HCl–MeOH. The reaction mixture was evaporated under reduced pressure to give a residue, which was passed through a Sephadex LH-20 column to remove the resultant salt. The oxidative products contained two components, which were separated by using silica gel column chromatography (Merck, Type 60) with $CHCl_3$–MeOH–H_2O (7 : 3 : 0.2) to afford **2** (2.14 g) and **3** (0.59 g).

Compound **2**, colorless needles, mp 204—207 °C. CD ($c = 5.35 \times 10^{-5}$, ethanol) $[\theta]^{24}$ (nm): -1.64×10^4 (294) (negative Cotton). IR ν_{max}^{KBr} cm^{-1}: 3400, 1735, 1710. MS (*m/z*): 413, 395 377, 213. FAB-MS (*m/z*): 1069.0 $[M+Na]^+$.

Compound **3**, colorless needles, mp 268—271 °C. IR ν_{max}^{KBr} cm^{-1}: 3300, 1640. MS (*m/z*): 315, 314, 297, 296, 279,

TABLE I. ^{13}C-NMR Data for Methyl Protodioscin (**1**),[6] Compound **4** and Kryptogenin[5]

	1 (in pyridine-d_5)	**4** (in pyridine-d_5)	Kryptogenin (in $CDCl_3$)			**1** (in pyridine-d_5)	**4** (in pyridine-d_5)
Aglycone 1	37.7	37.2	37.2	3-*O*-Gly	1′	100.6	100.3
2	30.3	30.1	31.4		2′	80.1	78.7
3	78.6	77.8	71.3		3′	76.7	76.9
4	40.1	38.6	42.1		4′	78.3	78.0
5	141.3	140.7	141.2		5′	77.9	77.9
6	121.7	121.4	120.6		6′	61.9	61.3
7	32.3	31.9	31.7	Rha	1″, 1‴	101.9, 103.1	102.0, 102.9
8	31.9	31.0	31.0		2″, 2‴	72.8, 72.9	72.6, 72.8
9	50.7	50.0	49.7		3″, 3‴	2 × 72.4	72.4, 72.5
10	37.4	37.1	36.6		4″, 4‴	73.9, 74.3	73.8, 74.1
11	21.3	20.7	20.6		5″, 5‴	69.4, 70.7	69.5, 70.4
12	40.7	40.4	39.6		6″, 6‴	18.3, 18.5	18.5, 18.6
13	41.0	41.7	41.7	26-*O*-Glc	1⁗	104.8	
14	56.9	51.1	51.2		2⁗	75.2	
15	32.5	38.9	38.6		3⁗	78.6	
16	81.5	217.7	218.1[a]		4⁗	72.3	
17	64.4	66.4	66.2		5⁗	78.1	
18	16.3	15.6	15.4		6⁗	63.3	
19	19.5	19.4	19.4	OMe		47.4	
20	39.2	43.7	43.3				
21	16.0	12.8	12.9				
22	112.9	213.3	214.4[a]				
23	31.0	37.4	37.0				
24	28.5	27.7	26.3				
25	34.4	36.1	35.2				
26	75.2	67.4	67.3				
27	17.2	17.3	16.7				

a) Assignments for signals due to C-16 and -22 in the preceding paper[5b] should be corrected as shown in this Table.

253. FAB-MS (*m/z*): 807.8 $[M+K]^+$, 791.6 $[M+Na]^+$. ^{13}C-NMR (pyridine-d_5)δ: 37.3, 30.1, 77.8, 38.9, 141.2, 121.6, 32.3, 31.8, 50.7, 37.1, 20.8, 46.2, 30.3, 56.4, 35.1, 155.2, 144.9, 15.9, 19.3, 196.4, 27.2 (C_1—C_{21}); sugar part, 100.2, 78.6, 76.8, 78.1, 77.8, 61.2 ($C_{1'}$–$C_{6'}$), 102.8, 101.9 ($C_{1''}$, $C_{1'''}$), 72.7, 72.6 ($C_{2''}$, $C_{2'''}$), 72.4 ($C_{3''}$, $C_{3'''}$), 74.0, 73.8 ($C_{4''}$, $C_{4'''}$), 70.3, 69.4 ($C_{5''}$, $C_{5'''}$), 18.6, 18.4 ($C_{6''}$, $C_{6'''}$).

Kryptogenin 3-*O*-β-Chacotrioside (4)——Compound **2** (2.14 g) was dissolved in dist. water (30 ml), and the solution was incubated with β-glucosidase (70 mg) at 36 °C for 24 h. After usual work-up, the product was recrystallized from dil. MeOH to provide colorless needles (1.44 g) of **3**, kryptogenin 3-*O*-β-chacotrioside, mp 231—234 °C. FAB-MS (*m/z*): 923.6 $[M+K]^+$, 907.9 $[M+Na]^+$. CD ($c=4.75\times10^{-5}$, ethanol) $[\theta]^{20}$ (nm): -1.79×10^4 (294) (negative maximum). IR ν_{max}^{KBr} cm^{-1}: 3400, 1735, 1710.

References and Notes

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