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HISPIGENIN, A NOVEL 22βO-SPIROSTANE FROM SOLANUM HISPIDUM[1]

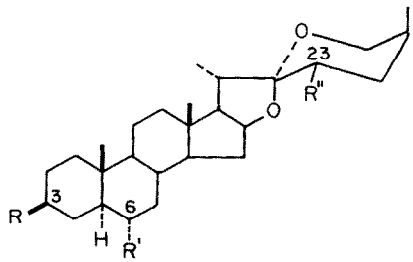
Ajit K. Chakravarty, Tarun K. Dhar and Satyesh C. Pakrashi*

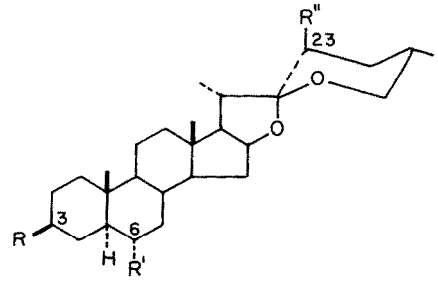
Indian Institute of Experimental Medicine, Jadavpur, Calcutta700032, India

The naturally occuring spirostane sapogenins known so far possess the 22αO-stereochemistry, though the 22βO isomers have been prepared[2] synthetically. We now report the isolation and structure elucidation of a 22βO-spirostane, hispigenin, from the leaves of S.hispidum.

The alcoholic extract of the leaves yielded (1.5%) the major glycoside, crystallised from acetone-methanol as flakes, m.p. 260-262° with shrinkage at 210°, $[\alpha]_D$ -61.53° (Py) besides β-sitosterol and its β-D-glucoside. Hydrolysis of the major glycoside with Kiliani mixture (AcOH:HCl:H_2O, 1.5:3.5:5) and paper chromatography showed the presence of L-rhamnose. That it is a birhamnoside was evident from the mass spectrum of its peracetylated product (glass) (m/e 503 and 273 for peracetylated birhamnose and rhamnose moieties respectively). Its hydrolysis to aglycone with acid proved to be impracticable as it led to an inseparable mixture of several components presumably by dehydration and rearrangements. Smith degradation[3] ($NaIO_4$ oxidation-$NaBH_4$ reduction-mild acid treatment) of sugar moiety gave a monorhamnoside [m/e 804 (M^+) and 273 for peracetylated product] indicating that the two rhamnose units were coupled through (1 → 3) linkage. The second rhamnose unit could then be hydrolysed by the same procedure to obtain a mixture of products from which three pure compounds, viz. neochlorogenin (Ia), $C_{27}H_{44}O_4$ (M^+ at m/e 432), paniculogenin (IIa), $C_{27}H_{44}O_5$ (M^+ at m/e 448) and a novel sapogenin, hispigenin (IIIa), $C_{27}H_{44}O_5$ (M^+ at m/e 448) could be separated by repeated chromatography over silicagel. The physical constants of these compounds and their derivatives are given in Table I. The structures of Ia and IIa were established by physical methods and finally by direct

comparison[4] with the authentic specimens.





1a, R=R'=OH, R"=H_2 IIa, R=R'=R"=OH IIIa, R=R'=R"=OH
1b, R=R'=OAc, R"=H_2 IIb, R=R'=R"=OAc IIIb, R=R'=R"=OAc
Ic, 3,6-diketo, R"=H_2 IIc, 3,6,23-triketo IIIc, 3,6,23-triketo

Hispigenin formed a triacetate (IIIb, M^+ at m/e 574) at room temp. and could be converted to a triketone (IIIc, M^+ at m/e 442) indicating that it contains three secondary OH groups. It showed IR bands at 982, 930, 900 and 868 cm^{-1} characteristic[6] of spirostanering system. The mass spectrum of IIIa, almost superimposable on that of IIa, exhibited intense peaks at m/e 363, 345, 327, 289, 271 and 253. It was therefore apparent that IIa and IIIa are stereoisomeric and the M^+ -85 peak at m/e 363 characterised[7] both of them as 23-hydroxy-spirostanes.

The PMR data summerised in Table II showed that hispigenin (IIIa) contains (a) an equatorial 27-Me as would be evident[8,9] from its chemical shift (δ 0.80 in $CDCl_3$ and δ 0.70 in Py) as well as from the nature and position of the signal for 26-H_2 (a broad doublet at δ 3.58 in Py and δ 3.33 in $CDCl_3$), (b) an α-oriented 21-Me since no deshielding of both 18-Me and 21-Me was observed[9,10], (c) an axial OH group at C-23 ($W_{1/2}$ = 13 Hz for 23-H which appeared as a broad doublet in Py) and (d) a 3β,6α-dihydroxy system as in Ia and IIa (cf. the chemical shifts of 19-Me of the compounds in Table II). Furthermore, the downfield shift of resonance frequency of 16-H of hispigenin (δ 5.16 in Py and δ 4.65 in $CDCl_3$) compared to that of IIa (δ 4.56 in Py and δ 4.50 in $CDCl_3$) and the upfield shift of the same signal for the triketone IIIc compared to that for IIc by 0.50 ppm clearly demonstrated a change[9] in the polar sites in the E/F ring system. Presumably, unlike the normal 22α<u>O</u>-configuration in paniculogenin (IIa) and all other naturally occurring spirostane derivatives, hispigenin possesses 22β<u>O</u>-stereochemistry as shown in IIIa. This was indeed supported by the pronounced shift[11] towards positive rotation of hispigenin

Table I. Physical constants of Ia, IIa, IIIa and their derivatives

Compound	m.p.	$[\alpha]_D$	Compound	m.p.	$[\alpha]_D$
Ia	252-256°	-50.8° (Py)	IIc	242-244°	-76.7° ($CHCl_3$)
Ib	202-204°	-35.2° (Py)	IIIa	258-260°	+23.3° (Py)
Ic	237-238°	-	IIIb	226-227°	+6° (Py)
IIa	222-224°	-62.5° (Py)	IIIc	240-244°	-23.8° ($CHCl_3$)
IIb	Amorphous, 112-118°	-53.5° (Py)			

Table II. PMR data (δ)* of sapogenins and their derivatives

Compound (solvent)	19-Me	18-Me	21-Me	27-Me	26-H_2	16-H	23-H	3-H & 6-H	OAc
Ia(Py)	0.83	0.86	1.12d (7)	1.05d (7)	3.30d(11), 3.39dd(11,3)	4.45ddd (7,7,7)	-	3.70m	-
IIa	0.82	0.78	0.97d (6)	1.07d (6)	3.23d(10) 3.83d(10)	4.40m	3.50m	3.50m	-
IIa(Py)	0.82	1.00	1.17d (7)	1.09d (7)	3.27d(11), 3.95dd(11,3)	4.56ddd (8,8,8)	5.95m	3.70m	-
IIIa	0.83	0.87	1.17d (7)	0.80d (7)	3.33d(10)	4.65m	3.50m	3.50m	-
IIIa(Py)	0.86	1.02	1.47d (7)	0.70d (6)	3.58d(7)	5.16ddd (8,8,8)	5.90d (7)	3.90m	-
Ib	0.90	0.77	0.98d (7)	1.08d (7)	3.30d(11), 3.97dd(11,3)	4.42m	-	4.70m	2.05
IIb	0.90	0.79	0.98d (7)	1.16d (7)	3.23d(11), 3.91dd(11,3)	4.46m	5.04dd (11,5)	4.62m	2.03, 2.04
IIIb	0.91	0.86	0.97d (7)	0.81d (7)	3.40d(11)	4.67m	4.67m	4.67m	2.03,2.04, 2.05
IIc	0.98	0.82	0.98d (7)	1.07d (7)	3.40d(12), 4.25dd(12,3)	4.65m	-	-	-
IIIc	0.96	0.86	0.96d (6)	1.05d (6)	3.72d(9)	4.15ddd (7,7,7)	-	-	-

*Recorded in a 90 MHz instrument except for IIb and IIIb for which 270 MHz machine was used. Figures in parentheses indicate J values in Hz.Unless otherwise stated, the spectra were taken in $CDCl_3$.

and its derivatives (Table I) compared to IIa and its corresponding derivatives. Moreover, the CD spectrum of the triketone IIIc showed negative Cotton effects between 290 and 320 nm. Since the 23-keto group in 22α-spirostane shows[5] very strong positive Cotton effect in this region, IIIc must have 22β-stereochemistry.

The structure and stereochemistry of hispigenin as IIIa could finally be confirmed by its isomerisation[12] to IIa on treatment with 6N ethanolic HCl at room temp. for 2 hr.

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References & Notes

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