Journal of Natural Products
Vol. 46, No. 5, pp. 614-618, Sep-Oct 1983

SCABROSIDOL, A NEW HIGHLY OXYGENATED IRIDOID GLUCOSIDE FROM *DEUTZIA SCABRA*

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ABSTRACT.—The structure and stereochemistry of 5β,7α-dihydroxy-deutziol have been demonstrated—by ^{13}C-nmr data and simple transformation into its mono-O-isopropylidene derivative—for scabrosidol **4**, a new highly polar iridoid glucoside isolated from *Deutzia scabra* (Saxifragaceae).

In the course of a systematic re-investigation of iridoid glucosides of *Deutzia scabra* (Saxifragaceae), we isolated—in addition to known deutzioside **1** (1), scabroside **2** (2), deutziol **3** (3), and more recent free aglycones (4) of **1** and **2**—a highly polar compound, present in small amounts, which we named scabrosidol **4**.

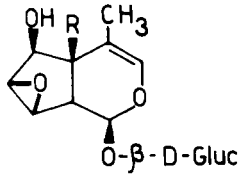
RESULTS AND DISCUSSION

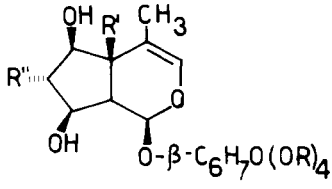
Compound **4** is an amorphous compound with molecular formula $C_{15}H_{24}O_{11}$ and $[\alpha]^{25}D-109°$. It gave, with vanillin reagent, a brown color similar to that of **2**, occurring in the same plant, and a negative Ross test (5) for the oxirane function.

By enzymatic hydrolysis with β-glucosidase, **4** gave D-glucose (1 mol), thus permitting the identification of the compound as a β-D-glucopyranoside, as supported by the typical doublet (δ 4.75, $J_{1',2'}=7.5$ Hz) of the anomeric H-1′. Its uv and ir spectra showed absorptions at 218 nm (log $\epsilon=3.8$) and 1670 cm^{-1}, respectively, both characteristic of a non-conjugated iridoid enol-ether system.

The ^{1}H-nmr spectrum of **4** (table 1) showed a close resemblance to those of natural deutziol **3** and synthetic 5β-hydroxy-deutziol **5**[1] (table 1) except for the general lacking in **4** of 2H-7 upfield signals and, only with respect to **3**, also of H-5 resonance.

All previous data would indicate for **4**, disregarding the stereochemistry, a structure of 7-hydroxy derivative of **5**. The comparison of ^{13}C-nmr spectra (table 2) of **5** and **4** (showing 15 distinct lines) confirmed for the latter compound the proposed structure. In fact, the resonances of corresponding carbons were in good agreement, apart from the lack in **4** of the characteristic triplet (SFORD) at 39.82 ppm of C-7 of **5** and the presence, as counterpart signal, of a doublet at 78.34 ppm arising from a hydroxymethine





1 R=H

2 R=OH

3 R=R′=R″=H

4 R=H, R′=R″=OH

5 R=H, R′=OH, R″=H

[1]The name we suggest for this synthetic compound, previously cited as 4-methyl-nor-harpagide (3), arises from its close structural analogy with **3**.

carbon. As regards the stereochemistry of **4**, the low field values of resonances of hydroxymethine C-6 (81.27 ppm) and C-7 (78.34 ppm) indicate a *trans*-1,2-diol arrangement of these hydroxyl functions, well supported by analogous values previously observed for cynanchoside (6) (C-6, 82.53 ppm; C-7, 78.90 ppm) and 7-α-hydroxyharpagide (7) (C-6, 82.64 ppm; C-7, 78.92 ppm), both having this typical *trans*-1,2-diol function.

To establish the correct relative orientation of the four hydroxyl groups in the aglycone unit, **4** was reacted with acetone-dimethylketal-$SnCl_2$, which afforded the unique O-isopropylidene derivative **6**.

The ^{1}H-nmr spectrum of **6** (table 1), compared with that of **4**, showed the presence of only one O-isopropylidene group (sharp three-proton singlets at δ 1.44 and 1.30, respectively) but did not furnish useful clues for an unambiguous placing of isopropylidene unit.

TABLE 1. ^{1}H-nmr shift assignments

Compound	H-1	H-3	H-5	H-6	H-7	H-8	H-9	H-11	Isopr.
1[a]	4.80 d	6.15 m	2.07 t	4.12 dd	3.62 dd	3.73 d	2.55 dd	1.64 s	
D_2O	$H_{1,9}$=10.0		$J_{5,6}$=7.5	$J_{5,6}$=7.5	$J_{6,7}$=1.5	$J_{7,8}$=2.5	$J_{1,9}$=10.0		
			$J_{5,9}$=7.5	$J_{6,7}$=1.5	$J_{7,8}$=2.5		$J_{8,9}$=7.5		
2[b]	5.12 d	6.25 q		4.33 d	3.9-3.7	3.9-3.7	2.62 d	1.62 d	
D_2O	$J_{1,9}$=9.2	J=1.0		$J_{6,7}$=1.5			$J_{1,9}$=9.2	J=1.0	
3[c]	5.40 d	6.01 m	2.7-2.2	4.4-3.5	2.7-1.1	4.4-3.5	2.7-2.2	1.60 d	
D_2O	$J_{1,9}$=1.5								
4	5.56 d	6.15 d		4.0-3.4	4.0-3.4	4.0-3.4	2.28 dd	1.58 d	
D_2O	$J_{1,9}$=1.5	J=1.5					$J_{1,9}$=1.5	J=1.5	
							$J_{8,9}$=11.5		
5[c]	5.57 d	6.06 d		4.4-3.6	2.5-1.3	4.4-3.6	2.41 dd	1.55 d	
D_2O	$J_{1,9}$=1.8	J=1.5					$J_{1,9}$=1.8	J=1.5	
							$J_{8,9}$=7.5		
6	5.66 d	6.38 d		4.28 d	4.10 dd	3.8-3.4	2.48 dd	1.52 d	1.44(3H)
D_2O	$J_{1,9}$=1.5	J=1.8		$J_{6,7}$=3.5	$J_{6,7}$=3.5	$J_{7,8}$=8.0	$J_{1,9}$=1.5	J=1.5	1.30(3H)
					$J_{7,8}$=8.0	$J_{8,9}$=11.5	$J_{8,9}$=11.5		
7	5.35 d	6.22 d		4.18[d] d	*ca.* 5.3[e] dd	*ca.* 5.1[e] dd	2.75 dd	1.63 d	1.52(3H)
$CDCl_3$	$J_{1,9}$=1.5	J=1.8					$J_{1,9}$=1.5	J=1.5	1.33(3H)
							$J_{8,9}$=11.0		

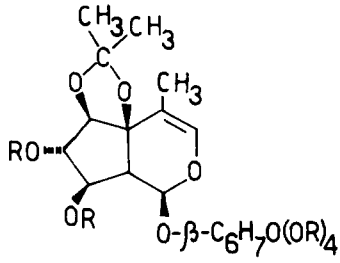
[a]From ref. (1).
[b]From ref. (2).
[c]From ref. (3).
[d]Overlapped to two of eight lines of CH_3OAc of D-glucose moiety, AB part of an ABX system where X=H-5′ on its turn further coupled.
[e]These assignments have been made tentatively by spin decoupling and are approximate.

Anyway, in the region between δ 4.3 and 3.4, the resonances of three aglycone hydroxymethine protons can be identified: a simple doublet of H-6 at δ 4.28 ($J_{6,7}$=3.5 Hz), a double doublet of H-7 at δ 4.10 ($J_{6,7}$=3.5 Hz, $J_{7,8}$=8.0 Hz), and a further double doublet at ca. δ 3.6 overlapped to glucose signals and tentatively assigned to H-8.

The acetylation of **6** in mild conditions led to the hexaacetate (peracetate) **7** whose ^{1}H-nmr spectrum (table 1), besides six distinct singlets of as many acetyl groups, made evident in the above region 4.3-3.2 only one residual aglycone resonance (δ 4.18) whose simple doublet multiplicity permits its unequivocal assignment to the H-6 proton, which evidently did not undergo any acetylation shift.

The identification of H-7 and H-8 resonances, clearly shifted downfield by acetylation effect, have been performed by double resonance experiments. The irradiation of H-9 resonance (δ 2.75) modified either the H-1 small doublet at δ 5.35 into a sharp singlet or the pattern of signals in the region δ 5.3-4.9, permitting us to locate the H-8 resonance there.

The last assignment was confirmed by irradiating within the cited region (at δ 5.1),



6 R=H

7 R=Ac

which simplified, as expected, the double doublet of H-9 into a narrow doublet with a small residual coupling $J_{1,9}=1.5$ Hz.

The collapsing of the small doublet at δ 4.18 (H-6) into a singlet, performed by shifting the irradiation frequency at δ 5.3, established the latter as the chemical shift value of H-7. The results of these double resonance experiments indicate that the O-isopropylidene unit must be located at C-5/C-6.

This was definitely proved by the ^{13}C-nmr spectrum of **7** (table 2) on the basis of significative deshielding values we previously observed (6) for iridoidic carbons involved in a ketal function; in fact, the deshielding values observed, with respect to **4**, for C-5 ($\Delta\delta=11.65$) and C-6 ($\Delta\delta=2.92$) are in agreement with those reported for the corresponding carbons of 5,6-8,10-bis-O-isopropylidene cynanchoside.[2]

The structure of **4** demonstrated a *cis*-relationship between OH functions at C-5

TABLE 2. ^{13}C-nmr chemical shifts

Compound	**1** D_2O	**2**[a] D_2O	**3** D_2O	**4** D_2O	**5** D_2O	**7**[b] $CDCl_3$
C-1	96.79 d	96.88 d	94.73 d	93.09 d	94.36 d	90.21 d
C-3	135.75 d	137.89 d	134.61 d	135.74 d	137.30 d	137.61 d
C-4	113.48 s	115.65 s	113.23 s	116.04 s	113.66 s	112.62 s
C-5	41.12 d	74.52 s	42.00 d	67.99 s	70.51 s	79.64 s
C-6	78.52 d	77.06 d	74.36 d	81.27 d	74.25 d	84.19 d
C-7	59.68 d	59.78 d	44.04 t	78.34 d	39.82 t	79.33 d
C-8	56.24 d	56.07 d	72.70 d	72.21 d	70.51 d	75.87 d
C-9	42.68 d	50.79 d	49.13 d	53.22 d	55.29 d	50.36 d
C-11	16.01 q	11.53 q	15.50 q	11.56 q	11.84 q	12.53 q
$\frac{Me}{Me}>C$						109.02 s
$\frac{Me}{Me}>C$						28.61 q 27.23 q
C-1′	100.00	99.80	99.11	98.87	99.21	94.37
C-2′	73.53	73.45	73.53	73.34	73.36	70.22
C-3′[c]	77.04	77.06	77.02	76.98	77.05	72.60
C-4′	70.32	70.33	70.45	70.52	70.51	68.29
C-5′[c]	76.57	76.48	76.49	76.18	76.26	72.24
C-6′	61.34	61.44	61.54	61.54	61.62	61.63

[a]From ref. (7).

[b]Additional signals from acetoxy groups at 170.31, 170.07, 169.99, 169.71, 169.10, 168.70 ppm (C=O) and 20.83, 20.74, 20.69, 20.54 ppm (CH_3).

[c]The assignments in vertical column could be reversed.

[2]The low deshielding value of C-5 in **7** could be ascribed to the influence of acetyl groups.

and C-6, both, therefore, β-oriented having always OH-5, a β-configuration. The non-formation of 6,7 or 7,8-mono-O-isopropylidene derivatives combined with ^{1}H- and ^{13}C-nmr data, confirmed the *trans*-relationship between OH-6 and OH-7 groups and thus, the α orientation of OH-7 and the β orientation of OH-8. The configuration of the latter chiral center is corroborated also by the "identity" of C-9 resonances in **4** and **5**, the slight difference of 2.07 ppm being due to the presence in **4** of the hydroxyl group at C-7, which exerts the well-known small shielding γ effect (*ca.* 2 ppm) (7).

Thus, to scabrosidol **4** must be attributed unambiguously the structure and configuration of 5β,7α-dihydroxy-deutziol. Because **4** is one of the two *trans* 7,8 diols that may arise from SN_2 cleavage of the oxirane ring of **2**, we took into consideration the possibility that **4** could be an artifact.

This hypothesis must however, be, ruled out, inasmuch as **4** was constantly present in all extracts investigated, which we prepared immediately after the collection of vegetal material on different samples and in different conditions (duration of extraction, pH, and evaporation temperature).

EXPERIMENTAL[3]

PLANT MATERIAL.—Fresh aerial parts of *Deutzia scabra* (Saxifragaceae) were collected in July 1981 in the Botanical Garden of the University of Rome. A reference specimen has been deposited in the herbarium of the same Botanical Institute (Voucher A-11).

EXTRACTION AND SEPARATION OF IRIDOID FRACTION.—The extraction of *Deutzia scabra* (6.4 kg) was performed as described in a previous paper (4). Compound **4** (Rf 0.12, brown spot with vanillin reagent) corresponds to compound **A** of fraction *c*.

ISOLATION OF SCABROSIDOL (**4**).—Fraction *c* (10 g) was chromatographed on silica gel (300 g). Elution with n-butanol saturated with water gave, in the first fractions, **1,3,2** (3 g), and finally a mixture of **2** and **4** (1 g).

The latter fraction, twice rechromatographed on silica gel in dichloromethane-methanol-water (DMW) 7:3:0.3 gave **2** (500 mg) and pure **4** (150 mg) as a hygroscopic amorphous powder; $[\alpha]^{25}D - 109°$ (*c* 1.0, MeOH); uv, λ max (MeOH), 218 nm (log ε 3.8); ir, ν max (3400, 2920, 1670, 1080, and 1020) cm^{-1}.

Anal. Calcd for $C_{15}H_{24}O_{11}$: C, 47.37; H, 6.36. Found: C, 47.15; H, 6.43%.

REDUCTION OF SCABROSIDE PENTAACETATE WITH $LiAlH_4$ TO 5β-HYDROXY-DEUTZIOL **5**.—Scabroside pentaacetate (**2**) (120 mg) was dissolved in dry tetrahydrofuran (10 ml) and then treated with $LiAlH_4$ (60 mg) at 70° and stirred for 6 h.

After cooling the mixture in an ice-bath, methanol was added (3 ml), and the solution was neutralized with 6 N HCl. After addition of water (8 ml) the solution was evaporated to an aqueous suspension that was treated with charcoal and stratified on a gooch funnel. After the salts had been removed with water, elution with ethanol gave a residue (60 mg) that was chromatographed on silica gel (12 g) in chloroform-methanol-water (7:3:0.3) to give scabroside **2** (10 mg) and 5β,7α-dihydroxy-deutziol **5** (40 mg).

The physical data (^{1}H-nmr, [α]D, Rf, reaction to vanillin) of **5** were in perfect agreement with those previously reported (3).

5,6-*O*-ISOPROPYLIDENESCABROSIDOL (**6**).—Scabrosidol (**4**, 120 mg) suspended in 0.5 ml of dry acetone was treated with a 15% solution of anhydrous $SnCl_2$ in dry acetone (2 ml), and acetone-dimethylketal (0.05 ml) was added.

The suspension was stirred for 1.5 h at room temperature and then poured into a cold, saturated solution of $NaHCO_3$ (100 ml). The resulting suspension was centrifuged and the residue was washed with acetone-water (1:1). The collected solutions showed, on tlc in DMW 8:2:0.2, the presence of a predominant compound. The solvent was evaporated, and the residue, chromatographed on silica gel in DMW 8:2:0.2, afforded **6** (35 mg) as amorphous powder.

ACETYLATION OF **6**.—5,6-O-isopropylidenescabrosidol (**6**, 35 mg) was treated with pyridine (0.4 ml) and acetic anhydride (0.8 ml) at room temperature for 1 h. After adding methanol (3 ml), we left the solution for 30 min and evaporated it in vacuo to dryness. The residue, chromatographed on silica gel in ethylether-hexane 8:2, gave pure hexaacetate **7** (40 mg).

[3]General techniques were as described earlier (8).

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Received 10 August 1982