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XANTHONES FROM THE ROOTS OF *Swertia iberica*

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From the roots of *Swertia iberica*, together with the previously known swertiaperennin decussatin, gentiakochianin, and norswertianin, we have isolated two new xanthones — isogentiakochianin and swertiaiberin. On the basis of UV, IR, PMR, and mass spectroscopy, the structure of 1,3,8-trihydroxy-7-methoxyxanthone is proposed for isogentiakochianin, and that of 1,2,3-trihydroxy-7,8-dimethoxyanthone for swertiaiberin.

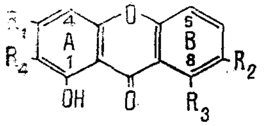
Plants of the genus *Swertia (Gentianaceae)* are of interest as a rich natural source of xanthone compounds. The chemical study of the xanthones in the plants of this genus began comparatively recently [1]. The increasing interest in xanthones is due to their pharmacological activity (stimulating action on the CNS [2] and cardiotonic [3] and tuberculostatic [4, 5] effects), and also to the fact that the qualitative composition and quantitative amount of xanthones are an important chemotaxonomic characteristic [6]. Within the framework of the study of domestic species of the genus *Swertia* we have undertaken a phytochemical investigation of *Swertia iberica* F. Fisch. et Mey, growing on the territory of the Georgian SSR.

On investigating a methanolic extract of the roots of *S. iberica* we isolated six individual substances belonging to the xanthone group (I-VI), two of which — (IV) and (V) — were new, and we have established the structures of these compounds.

Compound (I), from its composition ($C_{15}H_{12}O_6$), melting point (186-188°C), and UV-, IR, and PMR-spectroscopic characteristics corresponded to 1,8-dihydroxy-3,7-dimethaxyxanthone, which has been described previously under the names of swertiaperennin [7] and methylswertianin [8].

Compound (II), with the composition $C_{16}H_{14}O_6$, mp 156-158°C, according to spectroscopy, had the structure of 1-hydroxy-3,7,8-trimethoxyanthone and was identical with decussatin [7].

Compound (III), with the composition $C_{14}H_{10}O_6$, mp 223-226°C, according to spectroscopy,



I. $R_1 = OH, R_2 = R_3 = OCH_3, R_4 = H$
II. $R_1 = R_2 = R_3 = OCH_3, R_4 = H$
III. $R_1 = OCH_3, R_2 = R_3 = OH, R_4 = H$
IV. $R_1 = R_3 = OH, R_2 = OCH_3, R_4 = H$
V. $R_1 = R_4 = OH, R_2 = R_3 = OCH_3$
VI. $R_1 = R_2 = R_3 = OH, R_4 = H$

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had the structure 1,7,8-trihydroxy-3-methoxyxanthone and was identical with gentiakochianin [7] (swertianin [8]).

Compound (VI), with the composition $C_{13}H_{8}O_{6}$, mp 310°C, according to its spectroscopic characteristics, had the structure of 1,3,7,8-tetrahydroxyxanthone and corresponded to norswertianin [8].

Compounds (VI) and (V) were new, not having been described previously in the literature. We have called them isogentiakochianin and swertiaiberin, respectively.

Isogentikochianin (IV) with mp 235-238°C has the same composition, $C_{14}H_{10}O_{6}$, the same molecular weight of 274, and the same substituents as gentiakochianin (III) and differs from it only in the position of the methoxy group.

The UV spectrum of isogentiakochianin shows the four absorption maxima that are characteristic for the xanthone structure, $\lambda_{max}^{CH_3OH}$ 238, 256, 275 sh, 337, 385 nm, and in the presence of aluminum chloride a bathochromic shift of the shortwave maximum is observed which shows the presence of one or two free hydroxy groups in the α-position to the carbonyl group. In the presence of sodium acetate, unlike gentiakochianin, it showed a bathochromic shift of the long-wave maximum to the 337 nm region with a rise in its intensity, which is characteristic for an unsubstituted hydroxy group in position 3 [9] (Table 1).

The PMR spectrum of compound (IV) has four one-proton doublets at 6.58, 6.69 (J = 2.5 Hz, H-2, H-4), 6.92, and 7.50 ppm (J = 10 Hz, H-5,6), and also the signal of a methoxy group in the form of a singlet at 4.14 ppm. In the PMR spectrum of the acetate of compound (IV) there are three signals of acetyl groups, and singlets at 2.43 and 2.42 ppm indicate the presence of two acetyl substituents in the α-positions to the carbonyl group. An acetyl substituent in position 3 appears in the form of a singlet located in the stronger field – 2.33 ppm [10]. The correctness of the assignment of the signals of the acetyl substituents was checked on a model compound – the tetraacetate of 1,3,6,7-tetrahydroxyxanthone, which we obtained for these purposes by the hydrolysis of mangiferin and which has in its PMR spectrum three singlets in the region of acetyl groups: at 2.31 ppm, the acetyl group in position 3; at 2.34 ppm the two acetyl groups in positions 6 and 7; and at 2.47 ppm, the acetyl group in position 1.

On the basis of spectral characteristics, it may be concluded that isogentiakochianin is an isomer of gentiakochianin in which the methoxy group is present in position 7. It has the structure of 1,3,8-trihydroxy-7-methoxyxanthone.

Swertiaiberin (V) has the composition $C_{15}H_{12}O_{7}$, mp 231-234°C, M^+ 304. According to the PMR spectrum, the molecule of compound (V) contains five substituents, since two one-proton doublets are observed in the aromatic part of the spectrum at 7.64 and 7.81 ppm (J = 10 Hz), these being characteristic for protons in positions 5 and 6 (ring B), and in ring A there is one unsubstituted proton appearing in the form of a singlet at 6.82 ppm, the upfield shift of the signal being explained by the presence of substituents in positions 1, 2, and 3 [11]. Two of the five substituents are methoxy groups (singlets at 4.1 and 4.36 ppm), the upfield shift of one of the signals indicating the presence of a corresponding methoxy group in position 1 or 8. In ring A there is a hydroxy group in position 3, as is shown by the bathochromic shift in the 332 nm region in the presence of sodium acetate. The presence of a hydroxy group in position 1 is shown by a bathochromic shift of the shortwave maximum in the presence of aluminum chloride. The appearance of a bathochromic shift in the presence of sodium acetate and boric acid (ortho-dihydroxy grouping) and also a positive Bargellini reaction [12] shows that the third hydroxy group is in position 2. Thus, all three hydroxy groups in the swertiaiberin molecule are located vicinally in ring A.

Swertiaiberin has the structure of 1,2,3,-trihydroxy-7,8-dimethoxyxanthone.

EXPERIMENTAL

UV spectra were taken on a Specord UV-VIS instrument, IR spectra on a UR-20 spectrometer (paraffin oil), PMR spectra on a Varian HA-100D spectrometer, and mass spectra on a CH-8 mass spectrometer. Melting points were determined on a Kofler block. The elementary analyses of all the compounds corresponded to the calculated figures.

TABLE 1. UV Spectroscopic Characteristics of the Xanthones from *Swertia iberica* (nm)

Compound	+CH_3OH	+CH_3ONa	Δλ	+$AlCl_3$	Δλ	+$AlCl_3$ +HCl	Δλ	+CH_3COONa	Δλ	+CH_3COONa +H_3BO_3	Δλ
Swertiaperennin	239 m	243 h	+4	241 l	+2	240 l	+1	239 l	0	—	0
	264 h	273 l	+9	278 h	+14	278 h	+14	264 h	0	264 h	0
1,8 $(OH)_2$ 3,7	315 sh	—		332 l		330 l		320 sh		320 sh	
$(OCH_3)_2$ xanthone	331 m	342 l	+11	368 l	+37	369 l	+38	330 l	−1	330 m	−1
	386 l	412 l	+26	417 l	+31	418 l	+32	389 l	+3	389 l	+3
Decussatin	240 m	241 m	+1	238 m	−2	—		242 m	+2	—	
1 (OH) 3,7,8	262 h	262 h	0	276 h	+14	—		262 h	0	262 h	0
$(OCH_3)_3$ xanthone	315 m	317 m	+2	333 h	+18	333 h	+18	318 h	+3	318 h	+3
	380 l	385 l	+5	430 l	+50	418 l	+38	380 l	0	380 l	0
Gentiakochianin	241 m	252 l	+11	240 l	−1	242 l	+1	240 m	−1	—	
	270 h	276 h	+6	283 h	+13	274 h	+4	268 h	−2	273	+3
1,7,8 $(OH)_3$	322 sh	—		345 sh		330 sh		320 sh		320 sh	
3 (OCH_3) xanthone	332 h	333 l	+1	368 h	+36	365 l	+33	329 m	−3	329 m	−3
	395 l	418 l	+23	465 l	+70	455 l	+60	395 l	0	410 l	+15
Isogenetiakochianin	238 l	235 m	−3	265 l	+17	—		234 l	−4	—	
		246 sh						248 sh			
	256 m	273 h	+17	289 h	+33	—		275 m	+19	—	
1,3,8 $(OH)_3$	275 sh										
7 (OCH_3) xanthone	337 m	363 h	+26	337 l	0	329 l	−8	364 h	+27	346 m	+9
	385 l	—		376 l	−9	372 m	−13	—		—	
Swertiaiberin	238 m	—		238 m	0	240 h	+2	—		—	
1,2,3 $(OH)_3$	271 h	272 l	+1	304 h	+33	291 h	+20	295 m	+24	285 m	+14
7,8 (OCH_3) xanthone	332 m	—		362 m	+30	350 m	+18	356 l	+24	345 l	+13
	400 l	—		520 l	+120	490 l	+90	489 l	+89	425 l	+25
Norswertianin	239 m	—		246 m	+7	242 m	+3	—		—	
1,3,7,8 $(OH)_4$	268 h	266 l	−2	278 h	+10	276 h	+8	269 h	+1	272 h	+4
	321 sh			344 sh							
	331 h	345 m	+14	36[illegible] h	+31	363 h	+32	355 h	+24	330 h	−1
	390 l	—		4[illegible] l	+80	448 l	+58	—		405 l	+15
1,3,6,7 $(OH)_4$	240 l	—		235 h	−5	232 h	−8	—		—	
	257 h	270 m	+13	270 h	+13	266 h	+9	266 m	+9	261	+4
	270 sh	290 sh		288 sh		282 sh		—		—	
	315 m	—		359 m	+44	343 h	+28	340 l	+25	322 l	+7
	369 m	390 h	+21	427 h	+58	415 m	+46	400 h	+31	374 m	+5
										418 sh	

Notes. h) high; m) medium; *l*) low intensity of the absorption maximum; sh) shoulder.

Isolation of the Xanthones. The comminuted roots of *Swertia iberica* (3.0 kg) were extracted three times with six liters of methanol. The combined extracts were evaporated to the state of a syrup and this was treated with five liters of acetone; the amorphous precipitate that deposited was separated off, the acetone mother solution was evaporated and mixed with 250 g of silica gel, and the mixture was dried and subjected to separation on a column (silica gel "L" 100/400 μ). Elution was performed with petroleum ether (fractions 1-10), mixtures of petroleum ether and chloroform in ratios of 3:1 (fractions 11-16), 2:1 (fractions 17-21), and 1:1 (fractions 22-27), chloroform (fractions 28-33) and mixtures of chloroform and methanol with increasing concentrations of the latter. The volume of each fraction was about 200 ml.

Fractions 7-10 yielded substance (I) (swertiaperennin), fractions 12-14 substance (II) (decussatin), fractions 20-26, after reseparation on a column (Woelm polyamide; petroleum ether–chloroform with increasing concentrations of the latter) gave substances (III) (gentiakochianin) and (IV) (isogentiakochianin), fractions 27-28, after additional separation on polyamide, gave substance (V) (swertiaiberin), and fractions 28-33, by repeated recrystallization from chloroform–methanol (1:1) gave substance (VI) (norswertianin).

Acetylation of Substances (I-VI). About 0.05 g of one of substances (I-VI) was dissolved in 0.5 ml of pyridine, 1.0 ml of acetic anhydride was added, and after 24 h the mixture was poured into cold water with continuous stirring. The precipitate of the corresponding acetyl derivative was filtered off, washed repeatedly with water, and dried.

TABLE 2. Details of the PMR Spectroscopy of Xanthones from *Swertia iberica*

Compound	Magnitude of the chemical shift, δ, ppm (0 − TMS)								Solvent
	1	2	3	4	5,6	7	8	−OCH₃	
Swertiaperennin	OH	6,46 d J=2,5 Hz	OCH₃	6,52 d J=2,5 Hz	7,00 d 7,46 d J=10 Hz	OCH₃	OH	3,98s; 4,03s	TFA
Swertiaperennin acetate	2,42 s						2,42 s		TFA
Decussatin	OH	6,80 d J=2,5 Hz	OCH₃	6,93 d J=2,5 Hz	7,66 d 7,94 d J=10 Hz	OCH₃	OCH₃	4,12s; 4,45s	TFA
Decussatin acetate	2,50 s								CHCl₃
Gentiakochianin	OH	6,58 d J=2,5 Hz	OCH₃	6,63 d J=2,5 Hz	7,01 d 7,49 d J=10 Hz	OH	OH	3,99 s	TFA
Gentiakochianin acetate	2,42 s					2,33 s	2,42 s		CHCl₃
Isogentiakochianin	OH	6,58 d	OH	6,70 d J=2,5 Hz	6,92 d 7,49 d J=10 Hz	OCH₃	OH	4,14 s	TFA
Isogentiakochianin acetate	2,42 s	J=2,5 Hz					2,43 s		CHCl₃
Swertiaiberin	OH	OH	OH	6,82 d	7,64 d 7,81 d J=10 Hz	OCH₃	OCH₃	4,10s; 4,36s	TFA
Norswertianin	OH	6,24 d J=2,5 Hz	OH	6,38 d J=2,5 Hz	6,91 d 7,31 d J=10 Hz	OH	OH		DMSO
1,3,6,7-Tetrahydroxyanthone	OH	6,26 d J=2,5 Hz	OH	6,49 d J=2,5 Hz	6,96 d	OH	7,48 d		DMSO
1,3,6,7-Tetrahydroxyanthone acetate	2,47 s		2,31 s			2,34 s			CHCl₃

Notes. s) singlet; d) doublet; TFA) trifluoroacetic acid.

Preparation of 1,3,6,7-Tetrahydroxyxanthone. To 0.1 g of mangiferin (2-C-β-D-glucopyranosyl-1,3,6,7-tetrahydroxyxanthone) was added 0.6 g of phenol. With cooling, 1.0 ml of freshly distilled hydriodic acid (d 1.7) was carefully added to this mixture, and the whole was heated in a current of argon under reflux in the oil bath at 130°C for 7 h [13]. The cooled mixture was treated with 10 ml of water and was transferred to a column of polyamide and, after repeated washing with water, the 1,3,6,7-tetrahydroxyxanthone was eluted with methanol. The product was recrystallized from methanol—water (1:1). The yield of pure aglycone amounted to 43% of the theoretical figure. The compound obtained was acetylated by the method described above.

SUMMARY

Six xanthone compounds have been isolated from the roots of *Swertia iberica*, four of them having been described previously (swertiaperenin, decussatin, gentiakochianin, and norswertianin) and two being new (isogentiakochianin and swertiaiberin). The structure of 1,3,8-trihydroxy-7-methoxyxanthone is suggested for isogentiakochianin, and that of 1,2,3-trihydroxy-7,8-dimethoxyxanthone for swertiaiberin.

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