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TETRA AND PENTAOXYGENATED XANTHONES OF *SWERTIA LAWII*

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Key Word Index—*Swertia lawii*; Gentianaceae; 1,3,7,8-, 1,3,5,8-tetraoxygenated xanthones; 1-hydroxy-3,4,7,8-tetramethoxyxanthone; chemotaxonomy.

Abstract—1,3,7,8-Tetrahydroxyxanthone 1,7,8-trihydroxy-3-methoxyxanthone, 1,8-dihydroxy-3,7-dimethoxyxanthone, 1-hydroxy-3,7,8-trimethoxyxanthone, and 1-hydroxy-3,4,7,8-tetramethoxyxanthone have been identified in *Swertia lawii*. In addition, 1,3,5,8-tetrahydroxy- and 1-hydroxy-3,5,8-trimethoxyxanthone has been detected by analytical TLC. Chemotaxonomic significance of the polyoxygenated xanthones occurring in the *Swertia* is appraised.

INTRODUCTION

In connection with our work on xanthones of Gentianaceae, we undertook investigation of *Swertia lawii*, which is distributed in the mountains of the Western Peninsula and in the Nilgiris and is used as a substitute for *S. chirata* in the Indian system of medicine [1]. Previously, the isolation of erythrocentaurin from the whole plant was reported from this laboratory [2]. The isolation and identification of the polyoxygenated xanthones from the whole plant of *S. lawii* constitute the subject of this paper.

RESULTS AND DISCUSSION

The entire plants were milled and extracted for xanthones. The isolation and purification of the individual compounds were accomplished by solvent extraction, column chromatography, preparative layer chromatography and derivatization. The identity of the known compounds was established by spectral (UV, PMR, MS) evidence and by direct comparison with reference samples [3, 4]. The characterization of only the new naturally occurring xanthone, viz. 1-hydroxy-3,4,7,8-tetramethoxyxanthone, is described here.

* Part 15 in the series "Chemical Constituents of Gentianaceae". For Part 14 see Ref. [28].

1-Hydroxy-3,4,7,8-tetramethoxyxanthone (**3**). The compound, m.p. 192–194°, $C_{17}H_{16}O_7$ (M^+, 332), is a monohydroxytetramethoxyxanthone in which the hydroxyl group is strongly chelated, since it remained unaffected with ethereal diazomethane, but formed the permethyl ether with dimethyl sulphate and alkali. Its UV spectrum is characteristic of 1,3,4,7,8-pentaoxygenated xanthones [5, 6]. The 60 MHz PMR spectrum of the compound, in $CDCl_3$, showed one strongly chelated proton at 13·04 (C_1-OH), four methoxyl groups at δ 3·94–4·02, and three aromatic protons at δ 6·40 (1H, *s*, C_2–H), 7·05 (1H, *d*, *J* 9 Hz, C_5-H), 7·28 (1H, *d*, *J* 9 Hz, C_6–H). In the MS of the xanthone, aside from the molecular ion peak which is the base peak, significant fragment ion peaks appeared at *m/e* 317 (35%), 302 (48) 289 (20), 259 (10), associated with the loss of Me, CH_2O, C_2H_3O complex, and $CH_2O + C_2H_3O$ fragments, respectively. There were significant abundances of metastable ions to support the postulated rationalizations [3, 4; 6–8]. On the basis of the above observations, the pentaoxygenated xanthone is assigned 1-hydroxy-3,4,7,8-tetramethoxyxanthone structure (**3**), which was confirmed by direct comparison with an authentic synthetic sample.

Members of the genus *Swertia* are known to make 1,3,5,8- and 1,3,7,8-tetraoxygenated xanthones [3, 6, 9] but the occurrence of pentaoxygenated xanthones (1,3,4,5,8 and 1,3,4,7,8) in this genus was reported only once before (in *S. purpurascens*) [6]. The tetra and penta oxygenated xanthones occurring in *Swertia* were also encountered in *Gentiana* [5]. The close similarity between the polyoxygenated xanthones of the *Swertia* and those of the *Gentiana* seems to indicate a close relationship between the two genera. Members of the genus *Swertia* were initially identified with those of *Frasera* and *Halenia*. Subsequently, however, on the basis of elaboration of oxygenation patterns of the xanthonic constituents of a number of *Frasera* and *Halenia* species, a closer phytochemical relationship between the latter two than between either and *Swertia* was proposed [10]. Phytochemical examination of a number of *Swertia* species in the authors' laboratory, however, indicated that the above categorization is rather premature. Thus, *S. bimaculata* has been recently found [11] to contain polyoxygenated xanthones whose oxygenation and methylation patterns are closely similar to those of *Frasera albicaulis* [12] and *F. caroliensis* [13]. It is also interesting to note in this connection that marked variation in the relative abundance of 1,3,5,8- and 1,3,7,8-tetraoxygenated xanthones was observed in the members of the *Swertia* and *Gentiana*. The content of the two types of xanthones in several members of these two genera was found to be inversely proportional. In the present investigation of *S. lawii* also, the presence of the 1,3,5,8-tetraoxygenated xanthones

Table 1. The distribution of xanthones in Gentianaceae*: species: xanthones

Canscora decussata [4, 7, 8, 14]
1,5-$(OH)_2$-3-OMe, 1-OH-3,5-$(OMe)_2$, 1,5,6-$(OH)_3$-3-OMe, 1,3,6-$(OH)_3$-5-OMe, 1,3,5-$(OH)_3$-6-OMe, 1,6-$(OH)_2$-3,5-$(OMe)_2$, 1-OH-3,5,6-$(OMe)_3$, 1,3,7,8-$(OH)_4$, 1,3,8-$(OH)_3$-7-OMe, 1-OH-3,7,8-$(OMe)_3$, 1,3,5,6,7-$(OH)_5$, 1,3,7-$(OH)_3$-5,6-$(OMe)_2$, 1,6,7-$(OH)_3$-3,5-$(OMe)_2$, 1,7-$(OH)_2$-3,5,6-$(OMe)_3$, 1-OH-3,5,6,7-$(OMe)_4$, 1,3,6,7,8-$(OMe)_5$†, 1,3,5,6,7,8-$(OMe)_6$†.

Frasera albicaulis [12]
1,3,5-$(OMe)_3$, 1-OH-3,7-$(OMe)_2$, 1-OH-2,3,5-$(OMe)_3$, 1,3-$(OH)_2$-4,5-$(OMe)_2$, 1-OH-2,3,7-$(OMe)_3$, 1,3,7-$(OMe)_3$-2-OH, 1-OH-3,4,5-$(OMe)_3$, 1,3,4,5-$(OMe)_4$, 1-OH-3,4,7-$(OMe)_3$, 1,3,4,7-$(OMe)_4$, 1-OH-2,3,4,5-$(OMe)_4$, 1-OH-2,3,4,7-$(OMe)_4$, 1,3,4,7-$(OMe)_4$-2-OH, 1,2,3,4,7-$(OMe)_5$.

F. carliensis [13]
1-OH-2,3,5-$(OMe)_3$, 1-OH-2,3,7-$(OMe)_3$, 1,3-$(OH)_2$-4,5-$(OMe)_2$, 1,8-$(OH)_2$-3,5-$(OMe)_2$, 1-OH-2,3,4,5-$(OMe)_4$, 1-OH-2,3,4,7-$(OMe)_4$, 1,2,3,5,8-$(OMe)_5$†.

Gentiana bellidifolia [5]
1,3,5,8-$(OH)_4$, 1,3,8-$(OH)_3$-5-OMe, 1,5,8-$(OH)_3$-3-OMe, 1,8-$(OH)_2$-3,5-$(OMe)_2$, 1,3,8-$(OH)_3$-4,5-$(OMe)_2$, 1,3,8-$(OH)_3$-4,7-$(OMe)_2$.

G. corymbifera [5, 15]
1,3,8-$(OH)_3$-4,5-$(OMe)_2$.

G. kochiana [16, 17]
1,7,8-$(OH)_3$-3-OMe, 1,3-$(OH)_2$-7,8-$(OMe)_2$, 1,7-$(OH)_2$-3,8-$(OMe)_2$, 1,7-$(OMe)_2$-3,8-$(OH)_2$, 1-OH-3,7,8-$(OMe)_3$.

G. lutea [18]
1,3,7-$(OH)_3$, 1,3-$(OH)_2$-7-OMe, 1,7-$(OH)_2$-3-OMe, 1-OH-3,7-$(OMe)_2$.

G. lutea × *G. hegetschwelerii* [19]
1,7-$(OH)_2$-3-OMe.

G. lutea × *G. purpurea* [20]
1,7-$(OH)_2$-3-OMe.

G. turkestanorum [21]
1,5,8-$(OH)_3$-3-OMe.

G. verna [20]
1-OH-3,7,8-$(OMe)_3$.

Halenia asclepidea (HBK) G. Don (tentative identification) [10]
1-OH-2,3,5-$(OMe)_3$, 1-OH-2,3,4,5-$(OMe)_4$, 1-OH-2,3,4,7-$(OMe)_4$.

Macrocarpaea glabra [22]
1-OH-3,7-$(OMe)_2$, 1-OH-3,7,8-$(OMe)_3$.

Swertia bimaculata [11, 23]
1,3-$(OH)_2$-4,5-$(OMe)_2$, 1,8-$(OH)_2$-3,5-$(OMe)_2$, 1,3,5-$(OMe)_3$-8-OH, 1-OH-3,7,8-$(OMe)_3$, 1,4-$(OH)_2$-2,3,7-$(OMe)_3$, 1-OH-2,3,4,5-$(OMe)_4$, 1-OH-2,3,4,7-$(OMe)_4$.

Table 1—*continued*

S. chirata‡ [3, 19]
1,3,5,8-$(OH)_4$, 1,3,8-$(OH)_3$-5-OMe, 1,5,8-$(OH)_3$-3-OMe, 1,8-$(OH)_2$-3,5-$(OMe)_2$, 1-OH-3,5,8-$(OMe)_3$, 1,3,7,8-$(OH)_4$, 1,7,8-$(OH)_3$-3-OMe, 1,8-$(OH)_2$-3,7-$(OMe)_2$, 1-OH-3,7,8-$(OMe)_3$.

S. decussata [24, 25]
1,7,8-$(OH)_3$-3-OMe, 1,3-$(OH)_2$-7,8-$(OMe)_2$, 1-OH-3,7,8-$(OMe)_3$.

S. dilatata [26]
1,3,7,8-$(OH)_4$.

S. gracilescens [26]
1,3,7,8-$(OH)_4$.

S. japonica [19, 27]
1,3,5,8-$(OH)_4$, 1,3,8-$(OH)_3$-5-OMe, 1,5,8-$(OH)_3$-3-OMe, 1,8-$(OH)_2$-3,5-$(OMe)_2$, 1,8-$(OH)_2$-3,7-$(OMe)_2$, 1,3,7,8-$(OH)_4$, 1,7,8-$(OH)_3$-3-OMe.

S. lawii§
1,3,5,8-$(OH)_4$, 1-OH-3,5,8-$(OMe)_3$, 1,3,7,8-$(OH)_4$, 1,7,8-$(OH)_3$-3-OMe, 1,8-$(OH)_2$-3,7-$(OMe)_2$, 1-OH-3,7,8-$(OMe)_3$, 1-OH-3,4,7,8-$(OMe)_4$.

S. nervosa [26]
1,7,8-$(OH)_3$-3-OMe, 1,7-$(OH)_2$-3,8-$(OMe)_2$, 1,8-$(OH)_2$-3,7-$(OMe)_2$, 1-OH-3,7,8-$(OMe)_3$.

S. perennis [20, 25]
1,5,8-$(OH)_3$-3-OMe, 1,8-$(OH)_2$-3,7-$(OMe)_2$.

S. pseudochinensis [19]
1,3,5,8-$(OH)_4$, 1,5,8-$(OH)_3$-3-OMe, 1,8-$(OH)_2$-3,5-$(OMe)_2$, 1,3,7,8-$(OH)_4$, 1,7,8-$(OH)_3$-3-OMe, 1,8-$(OH)_2$-3,7-$(OMe)_2$, 1-OH-3,7,8-$(OMe)_3$.

S. purpurascens‡ [28]
1,3,5,8-$(OH)_4$, 1,3,8-$(OH)_3$-5-OMe, 1,5,8-$(OH)_3$-3-OMe, 1,3,7,8-$(OH)_4$, 1-OH-3,7,8-$(OMe)_3$, 1-OH-3,4,5,8-$(OMe)_4$, 1-OH-3,4,7,8-$(OMe)_4$.

S. racemosa [26]
1,3,5,8-$(OH)_4$, 1,5,8-$(OH)_3$-3-OMe, 1,8-$(OH)_2$-3,5-$(OMe)_2$, 1,3,7,8-$(OH)_4$, 1,7,8-$(OH)_3$-3-OMe, 1,8-$(OH)_2$-3,7-$(OMe)_2$.

S. randaiensis [19]
1,3,5,8-$(OH)_4$, 1,3,7,8-$(OH)_4$, 1,7,8-$(OH)_3$-3-OMe.

S. swertopsis [19]
1,8-$(OH)_2$-3,5-$(OMe)_2$, 1,3,7,8-$(OH)_4$, 1,7,8-$(OH)_3$-3-OMe, 1,8-$(OH)_2$-3,7-$(OMe)_2$, 1-OH-3,7,8-$(OMe)_3$.

S. tosaensis [19]
1,3,5,8-$(OH)_4$, 1,3,8-$(OH)_3$-5-OMe, 1,5,8-$(OH)_3$-3-OMe, 1,8-$(OH)_2$-3,5-$(OMe)_2$, 1,3,7,8-$(OH)_4$, 1,7,8-$(OH)_3$-3-OMe, 1,8-$(OH)_2$-3,7-$(OMe)_2$.

* The distribution of glycoxanthones, glycoflavones and xanthone-*O*-glycosides in Gentianaceae has recently been reported [6]; † identified as the permethyl ether; ‡ denotes 1,3,5,8-tetraoxygenated xanthones occurring as the major constituents; § denotes 1,3,7,8-tetraoxygenated xanthones occurring as the major constituents.

could only be detected by TLC while the 1,3,7,8 and 1,3,4,7,8 patterns were obtained in high yields. This observation has a direct bearing on the biogenesis of polyoxygenated xanthones. Table 1 lists all the polyoxygenated xanthones that have been isolated so far from Gentianaceae (Table 1).

EXPERIMENTAL

The general procedures used are the same as reported in a recent paper [3].

Isolation of xanthones from S. lawii. Dried and milled whole plants (1·2 kg) were continuously extracted (24 hr) in a Soxhlet with light petrol. (60–80°) and the defatted plant material was then extracted with alcohol (24 hr). The two extracts were separately processed.

Treatment of petrol. extract. The petrol. extract was conc. (*ca* 500 ml) and the concentrate was kept overnight at ordinary temp. when a yellow amorphous solid (Fraction A, 4·3 g) separated. The solid was collected by filtration and the mother liquor was evaporated (Fraction B).

Separation of xanthones present in Fraction A. The solid (2·4 g), from Fraction A, was mixed with equal amount of silica gel and packed over a column (20 × 3 cm) of silica gel. C_6H_6 (8 l.) and $CHCl_3$ (4·1) were used as the eluents. Earlier C_6H_6 fractions gave a solid, m.p. 218–220° (0·47 g) which showed one major and one minor spots on TLC.

1,7,8,-Trihydroxy-3-methoxyxanthone (**1**). A portion of the above solid on repeated crystallizations from MeOH afforded yellow needles, m.p. 220°. The m.p., UV, PMR and MS of the compound were identical with those of 1,7,8-trihydroxy-3-methoxyxanthone [27]. The dimethyl ether, prepared with ethereal diazomethane, was identical with decussatin [4] in all respects.

Separation of xanthones present in Fraction B. The solid (12·8 g), from Fraction B, was dissolved in Et_2O (1 l.) and the

phenolic and neutral components were separated in the usual way [3]. The mixture of phenolic constituents (1·2 g) was chromatographed over silica gel column (18 × 3 cm) using light petrol. (1 litre), petrol.–C_6H_6 (1:1, 3 l.), C_6H_6 (2 l.), and $CHCl_3$ (3 l.). The light petrol. eluates gave only a small amount of an amorphous solid which was not processed further.

1,8-Dihydroxy-3,7-dimethoxyxanthone (**2**). The petrol.–C_6H_6 eluates, on conc, furnished a yellow solid (72 mg) which crystallized from EtOH as yellow needles, m.p. and mixed m.p. 185–186°. The co-TLC, UV and MS of the compound were also identical with those of 1,8-dihydroxy-3,7-dimethoxyxanthone [3]. Treatment of the compound with ethereal diazomethane gave decussatin (m.p., m. m.p., co-TLC). The middle benzene eluates showed one major and one minor spots on TLC. The two components were separated by preparative TLC using $CHCl_3$.

1-Hydroxy-3,4,7,8-tetramethoxyxanthone (**3**). The major component (preparative layer zone, $R_f \sim 0{\cdot}2$) was eluted with $CHCl_3$ from one chromatoplate. The residue, obtained from the $CHCl_3$ soln, crystallized from EtOH as yellow needles (12 mg), m.p. 192–194° (Ref. 5, m.p. 192–193°); UV: λ_{max} (EtOH) 240 (0·63), 262 (0·78), 270–275 *sh* (0·44), 312 (0·305), 380 nm (0·09). It was found to be identical with a synthetic sample of 1-hydroxy-3,4,7,8-tetramethoxyxanthone, prepared from decussatin by persulphate oxidation followed by methylation with ethereal diazomethane. The minor component (from the upper preparative layer zone, $R_f \sim 0{\cdot}5$), obtained in a similar way as above, was shown to be identical with 1-hydroxy-3,5,8-trimethoxyxanthone [3] by direct comparison (co-TLC, UV). The $CHCl_3$ eluates of Fraction B showed several spots on TLC and could not be disentangled due to their close R_f values and small quantity.

1-Hydroxy-3,7,8-trimethoxyxanthone (**4**). The solid (0·43 g) appeared at the Et_2O–H_2O interface, during separation of the phenolic constituents of Fraction B, was washed with dil. HCl and then with H_2O, and then dried. It crystallized from EtOH as yellow needles (112 mg), m.p. 148–149°. The m.p., m.m.p. R_f, and UV spectrum were identical with those of an authentic sample of decussatin.

Treatment of EtOH extract. The EtOH extract was conc. to a syrupy liquid. It was poured into aq. HOAc (4%, 400 ml.) and the mixture was kept at ordinary temp. overnight. The solid was collected by filtration and was kept for further processing for more polar compounds. The clarified acidic soln was extracted with Et_2O (10 200 ml portions) and the combined extracts was worked up for xanthones to give a yellow solid (3·4 g).

1,3,7,8-Tetrahydroxyxanthone (**5**). The above solid was repeatedly extracted with hot $CHCl_3$ (5 100 ml portions). The combined $CHCl_3$ extracts was conc. when a $CHCl_3$-sparingly soluble solid separated. The mother liquor was marked Fraction C. The solid crystallized from MeOH as light yellow micro needles (0·32 g), m.p. 328–339° (Ref. 27, m.p. 335°). The corresponding tri- and tetramethyl ethers, prepared in the usual way, were found to be identical, respectively, with decussatin [3] and 1,3,7,8-tetramethoxy xanthone [3]. The MeOH mother liquor, after separation of 1,3,7,8-tetrahydroxyzanthone, showed the presence of 1,3,5,8-tetrahydroxyxanthone (co-TLC, UV).

Separation of xanthones present in Fraction C. The $CHCl_3$ concentrate was chromatographed over silica gel (24 × 3 cm). Elution was carried out with C_6H_6 (3 l.), $CHCl_3$ (4 l.) and MeOH (4 l.). Fractions (500 ml) were collected. The C_6H_6, $CHCl_3$ and MeOH eluates on concn gave further crops of xanthones **4** (380 mg), **1** (222 mg), and **5** (178 mg), respectively.

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