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SAPXANTHONE, A PENTASUBSTITUTED XANTHONE FROM *SAPONARIA VACCARIA*

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Key Word Index—*Saponaria vaccaria*; Caryophyllaceae; xanthones; 1,8-dihydroxy-3,5-dimethoxy-7-[(*E*)-propenyl-7′-hydroxy-dodecanoate]-9H-xanthen-9-one, and 1,8-dihydroxy-3,5-dimethoxy-9H-xanthen-9-one.

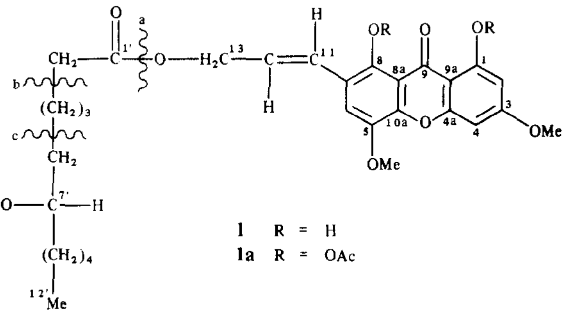
Abstract—Sapxanthone, a novel xanthone with a polyfunctional side chain, has been isolated along with 1,8-dihydroxy-3,5-dimethoxy-9H-xanthen-9-one from *Saponaria vaccaria*. Their structures have been elucidated through chemical and spectroscopic methods. This constitutes the first report of the natural occurrence of xanthones in the genera *Saponaria* and *Vaccaria*.

INTRODUCTION

Saponaria and *Vaccaria* species are reputed to possess analgesic, antigranulation [1] and antitumour activities [2], and are widely used in Armenian medicine [2]. One of these is *Saponaria vaccaria* (syn. *Vaccaria pyramidata*; *V. segetalis*; *V. hispanica*) which is an annual herb growing as a weed in cultivated fields in Northern Areas of Pakistan and also widespread in the flora of the U.S.S.R. [3]. It is reputed to possess sudorific, emetic and laxative properties and is also used in indigenous system of medicine for the treatment of jaundice, rheumatism, hepatic eruption and venereal ulcers [4]. Its toxicity against worms, *Paramecium*, and other unicellular organisms is also reported [5]. A literature survey showed that some saponins [6, 7], and terpenic- and flavonoidal-glycosides [8, 9] have so far been reported from this species. The medicinal importance attached to this plant prompted us to reinvestigate its chemical constituents for new biologically important compounds. This has now led to isolation of two xanthones from the methanolic extract of fresh and shade-dried stems of this plant. One of these is new and we have named it as sapxanthone (**1**). The other is 1,8-dihydroxy-3,5-dimethoxy-9H-xanthen-9-one, which has been reported previously from other plants [10–13].

RESULTS AND DISCUSSION

Xanthone **1**, $C_{30}H_{38}O_9$ (-ve FABMS, $[M]^+ = m/z$ 542). On acetylation, it formed a triacetate (**1a**) which showed a molecular ion peak at m/z 668 corresponding to the molecular formula $C_{36}H_{44}O_{12}$. Its IR spectrum showed absorptions for OH (3440–3200 cm^{-1}), ester (1720 cm^{-1}), conjugated carbonyl (1670–1650 cm^{-1}), conjugated C=C (1620 cm^{-1}) and OMe groups (1250 cm^{-1}). Its UV spectrum, λ_{max} at 334.0, 279.2, 255.6 and 230.8 nm, was characteristic of a 1,3,5,8-tetraoxygenated xanthone [10]. The insolubility of **1** in dilute sodium carbonate solution and the absence of a bathochromic shift of the K- band on addition of sodium acetate reflected the absence of OH groups at positions 3 and 5. In addition to the molecular ion peak, the mass spectrum showed peaks at m/z 527 $[M-Me]^+$ and 524 $[M-H_2O]^+$, beside prominent ions at m/z 288 and 287 representing the loss of a $C_{15}H_{27}O_3$ side chain with or without H transfer. Other peaks at m/z 273, 245 and 230 were characteristic of 1,3,5,8-tetraoxygenated xanthones [10].



1 R = H
1a R = OAc

In the ^1H NMR spectrum at 400 MHz, two sharp singlets of 1H each were observed at δ11.39 and 11.98, respectively. These disappeared on shaking with D_2O and could be assigned to chelated hydroxyl groups at positions 1 and 8. The sharp singlets of 3H each at δ3.89 and 3.95 were due to two methoxyl groups which were allocated to C-3 and C-5 considering the absence of a hydroxyl group at these positions. The presence of one pair of *meta*-coupled protons and one isolated proton in two different aromatic rings was also evident from the ^1H NMR which showed two aromatic protons exhibiting *meta*-split doublets at δ6.55 and 6.36 ($J = 2.28$ Hz). The xanthone **1** thus carries one hydroxyl- and one methoxyl-group at positions 1 and 3 in one of the aromatic rings leaving positions 6 and 7 for the side chain in the other aromatic ring. The isolated proton at δ7.25 could be assigned to C-6 on the basis of the chemical shift which showed complete agreement with that observed earlier by Sluis and Labadie [10] in related compounds. Sapxanthone is, therefore, derived from 1,8-dihydroxy-3,5-dimethoxy-9H-xanthen-9-one with an additional $C_{15}H_{27}O_3$ side chain at position-7. As a result of further studies the following structures were elucidated for sapxanthone **1** and its triacetylated product **1a**.

The evidence of the structure of side chain was provided by the ^{1}H- and ^{13}C NMR data and authenticated through selective homodecoupling experiments. The downfield one proton signals at δ5.36 and 5.28 were assigned to olefinic protons and a large *trans* coupling of 13.7 Hz between them revealed the *E* configuration. The methylene protons adjacent to ester oxygen were non-equivalent giving double doublets at δ4.28 and 4.14. Each of these showed a geminal coupling of 11.92 Hz and vicinal couplings of 4.32 and 5.96 Hz respectively. Irradiation of the signal at δ5.36 simplified the multiplet at δ5.28 into a *dd* ($J_{vic}=4.32$ and 5.96 Hz) while irradiation at δ5.28 caused the doublet at δ5.36 to collapse into singlet and simplified the double doublets at δ4.28 and 4.14 into doublets each with geminal coupling of 11.92 Hz. Irradiation at either δ4.28 or 4.14 simplified the multiplet at δ5.28 into a doublet showing *trans* vicinal coupling of 13.7 Hz. The signals at δ5.36 and 5.28, were therefore assigned to H-11 and H-12 and those at δ4.28 and 4.14 to the protons at C-13.

The triplet at δ2.30 was assigned to methylene protons adjacent to a carbonyl function and its multiplicity revealed the presence of another neighbouring methylene group. This part of skeleton was also reflected by prominent peaks in the mass spectrum at m/z 343, 385 and 199 which originated through cleavages 'a' and 'b', representing characteristic α- and β-cleavage reactions of esters. Sapxanthone is therefore an O-alkenyl ester of hydroxydodecanoic acid. The ^{1}H and ^{13}C NMR spectra indicated the rest of the carbons formed a straight chain terminating in an ethyl group (3H triplet at δ0.86 and 2H multiplet at δ1.40). The hydroxyl group was assigned to C-7′ on the basis of fragments triggered by the hydroxyl group. The elimination of either of the alkyl group from the secondary alcohol resulted in diagnostic fragments at m/z 101 and 441, out of which the former was predominant. Further support was provided by another diagnostic peak at m/z 426 representing simultaneous losses of H_2O and heptene molecules.

Xanthone **2**, $C_{15}H_{12}O_6$, was also a dihydroxy-dimethoxy xanthone. Its spectral properties (MS, UV, IR and ^{1}H NMR) as well as mp were in agreement with literature data for 1,8-dihydroxy-3,5-dimethoxy-9H-xanthen-9-one [10–13].

A careful search of the literature showed that complete assignments of various carbon atoms in the ^{13}C NMR spectra of 1,3,5,8-tetraoxygenated xanthones have not so far been made. This led us to carry out detailed ^{13}C NMR spectral studies on both **1** and **2**. The multiplicities of various carbon atoms were determined by DEPT experiments keeping the last pulse angle $\theta=45°$, 90°, 135°, and the number of quaternary carbons were determined by subtracting these from the broad band spectrum. The assignments were made on the basis of theoretical considerations and also by comparison with published spectra of xanthones [10, 14, 15] and long chain alcohols [16].

It is significant to note that in spite of an enormous amount of work reported on *Saponaria* and *Vaccaria* species, the present paper describes the first natural occurrence of xanthones from these genera and their isolation may be of chemotaxonomic significance.

EXPERIMENTAL

General. UV and IR: EtOH and $CHCl_3$, respectively; ^{1}H- and ^{13}C NMR: 400 MHz and 45 MHz respectively, $CDCl_3$, TMS as int. ref. The -ve FABMS were carried out on Finnigan MAT 112S Mass Spectrometer.

Plant material. The plant material was collected from Northern areas of Pakistan and was identified by the Department of Botany, University of Karachi.

Extraction and isolation. The plant material was extracted with MeOH at room temp. The residue obtained after the evapn of solvent was subjected to CC over silica gel and was eluted with various solvent gradients of increasing polarities. Compounds **1** and **2** were respectively eluted with n-C_6H_{14}–$CHCl_3$ (1:1) and (1:4), in pure crystalline forms.

Sapxanthone. Mp 198–200°, $[\alpha]_D+51.7$ ($CHCl_3$; c 1.2). UV and IR: see Results and Discussion; ^{1}H NMR: δ11.98 (1H, *s*, OH), 11.39 (1H, *s*, OH), 7.25 (1H, *s*, H-6), 6.55 (1H, *d*, $J=2.28$ Hz, H-4), 6.36 (1H, *d*, $J=2.28$ Hz, H-2), 5.36 (1H, *d*, $J=13.7$ Hz, H-11), 5.28 (1H, *m*), 4.28 (1H, *dd*, $J_{gem}=11.92$, $J_{vic}=5.96$ Hz), 4.14 (1H, *dd*, $J_{gem}=11.92$, $J_{vic}=4.32$ Hz), 3.95 (3H, *s*, OMe), 3.89 (3H, *s*, OMe), 3.60 (1H, *t*, OH), 2.30 (2H, *t*, 2′-H_2), 1.40 (2H, *m*, 11′-H_2), 1.25 (14H, *br s*), 0.86 (3H, *t*, 12′-Me); -ve FABMS m/z: 541 $[M-H]^-$, 526 $[M-H-Me]^-$, 523 $[M-H-H_2O]^-$, 440 $[M-H-C_6H_{13}O]^-$, 425 $[M-H-C_7H_{16}O]^-$, 384 $[M-H-C_{10}H_{21}O]^-$, 342 $[M-H-C_{12}H_{23}O_2]^-$, 287 $[M-H-C_{15}H_{26}O_3]^-$, 286 $[M-H-C_{15}H_{27}O_3]^-$, 272 $[M-H-C_{15}H_{26}O_3-Me]^-$, 244 $[M-H-C_{15}H_{26}O_3-C_2H_3O]^-$, 229 $[M-H-C_{15}H_{26}O_3-C_3H_6O]^-$, 198 $[M-H-C_{18}H_{15}O_7]^-$, 100 $[M-H-C_{24}H_{25}O_8]^-$; ^{13}C NMR: See Table 1.

Compound **1a**. Sapxanthone **1** (10 mg) was stirred 100° in C_5H_5N (1.5 ml) and Ac_2O (5.0 ml) for 30 min. The reaction mixture was worked-up in the usual manner to yield compound **1a** (6.3 mg) in pure crystalline form, mp 120–122°; $[\alpha]_D^{20}+15.7$ ($CHCl_3$; c 1.1). -ve FABMS m/z: 667 $[M-H]^-$; ^{1}H NMR ($CDCl_3$): δ7.18 (1H, *s*, H-6), 6.49 and 6.33 (each 1H, *d*, $J=2.28$ Hz), 5.32 (1H, *d*, $J=13.71$), 5.28 (1H, *m*), 4.27 (1H, *dd*, $J_{gem}=11.92$ Hz, $J_{vic}=4.32$ Hz), 4.14 (1H, *dd*, $J_{gem}=11.92$ Hz, $J_{vic}=5.96$ Hz), 3.93 and 3.88 (each 3H, *s*, OMe), 2.47, 2.43 and 2.35 (each 3H, *s*, Ac), 2.31 (2H, *t*, 2′-H_2).

Xanthone **2**. Mp 184–186°; UV λ_{max}^{EtOH} nm: 334.3, 302.1, 279.4, 255.3, 234.7; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450–3200 (OH), 1670–1640 (conjugated carbonyl), 1610 (conjugated C=C), 1240 (OMe);

Table 1. ^{13}C NMR data of compounds 1 and 2 ($CDCl_3$)

C	**1**	**2**		**1**
1	162.13	162.03	1′	174.0
2	97.93	97.62	2′	34.12
3	170.13	168.7	3′	24.84
4	93.14	93.31	4′	29.37
4a	156.40	158.8	5′	29.67
5	151.22	150.11	6′	29.46
6	109.32	117.83	7′	31.91
7	136.02	115.23	8′	68.84
8	153.0	155.83	9′	34.07
8a	104.15	102.35	10′	29.10
9	182.90	184.20	11′	22.66
9a	100.91	100.40	12′	14.07
10a	142.50	144.32		
OMe (3)	55.97	55.82		
OMe (5)	57.09	56.93		
11	134.21			
12	120.34			
13	62.09			

^{1}H NMR: δ11.98 (1H, *s*, OH), 11.43 (1H, *s*, OH), 7.25 (1H, *d*, *J* = 9.2 Hz, H-6), 6.73 (1H, *d*, *J* = 9.2 Hz, H-7), 6.52 (1H, *d*, *J* = 2.47 Hz, H-4), 6.39 (1H, *d*, *J* = 2.47 Hz, H-2), 3.93 (3H, *s*, OMe), 3.87 (3H, *s*, OMe); EIMS *m/z*: 288 $[M]^+$ ($C_{15}H_{12}O_6$), 273 $[M-Me]^+$, 245 $[M-C_2H_3O]^+$, 230 $[M-C_3H_6O]^+$.

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ALKALOIDS AND COUMARINS FROM STEM BARK OF *CITRUS GRANDIS*

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Key Word Index—*Citrus grandis f. buntan*; Rutaceae; acridone alkaloids; buntanmine-A; coumarins; buntansin.

Abstract—An acetone extract of the stem bark of *Citrus grandis. f. buntan* afforded a new acridone alkaloid, buntanmine-A and a new coumarin, buntansin, together with six known acridone alkaloids and 10 known coumarins. Structures were elucidated by spectral methods and chemical transformations.

INTRODUCTION

Citrus grandis f. buntan (Chinese name: Buntan) is a well known fruit belonging to the Rutaceae in Taiwan. In continuation of our chemical investigation of the genus *Citrus* [1], we were interested in the constituents of this species. Recently, we have reported on the isolation of novel skeletal homoacridone alkaloids, acridone alkaloids and coumarins from the root bark of the plant [1, 2]. Further examination of the stem bark has now resulted in the isolation of 18 compounds, two (**1** and **3**) of which are a new acridone alkaloid and a new coumarin, respectively. In this paper, we describe the structural determination of these compounds.

RESULTS AND DISCUSSION

Buntanmine-A (**1**) was obtained as yellowish granules, mp 201–202°, $[\alpha]_D$ −116.7° (MeOH). The molecular formula was determined as $C_{21}H_{23}NO_6$ by HR mass spectrometry. The UV spectrum of **1** showed similar absorptions to that of grandisinine (**8**), indicating the presence of a 9-acridone nucleus [3–6]. The bathochromic shifts of UV bands with shift reagents and IR bands at 3407 and 1614 cm^{-1} together with signals at δ14.28 and 6.40 (each 1H, disappearing with D_2O) in the ^{1}H NMR spectrum, indicated the presence of hydroxyl groups in **1** with at least one of them being strongly hydrogen bonded. The AB type signals in the ^{1}H NMR spectrum at δ6.95 and 8.01 (each 1H, *d*, *J* = 8.8 Hz) were attributed to mutually *ortho*-located aromatic protons, the lower field signal being assigned to H-8 in the

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