New Metabolites from *Onopordum illyricum*

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Received March 10, 1999

A phytochemical investigation of *Onopordum illyricum* afforded, in addition to several known compounds, two new eudesmane sesquiterpenes (**1** and **2**), two new elemane sesquiterpenes (**3** and **4**), and one new neolignan derivative (**5**). The structure elucidation of all compounds was based on their ^{1}H and ^{13}C NMR spectral data, including those derived from 1D TOCSY, 2D NMR, COSY−DQF, HSQC, and HMBC experiments, as well as extensive 1D ROESY studies.

Onopordum illyricum L. (Compositae, tribe Cynareae, subtribe Carduinae) is widely distributed along the Mediterranean coast of Italy where it grows wild and is called "Cardo maggiore".[1] Plants of the genus *Onopordum* have been employed traditionally for their antibacterial, hemostatic, and hypotensive properties.[2] Fresh extracts of *O. acanthium* have been used topically to treat skin cancers.[3] Several species of the genus *Onopordum* have been investigated chemically, with flavonoids,[4] lignans,[4] and sesquiterpene lactones[5] being the most characteristic constituents.

In the present paper, we report the isolation and structure elucidation of two eudesmanes (**1** and **2**), two elemanes (**3** and **4**), and one neolignan (**5**), from the hitherto unstudied *O. illyricum* (Chart 1). Also isolated and identified from the $CHCl_3$- and MeOH-soluble extracts of this plant were several known compounds.

Results and Discussion

The dried flowers of *O. illyricum* were extracted successively with *n*-hexane, $CHCl_3$, $CHCl_3$−MeOH (9:1), and MeOH. The $CHCl_3$ extract was chromatographed on a Si gel column followed by HPLC purification to give the sesquiterpenes **1**−**4**, the neolignan **5**, and the known sesquiterpenes onopordopicrin,[6] carmanin,[7] 4-*epi*-carmanin,[7] elemacarmanin,[7,16] 8α-sarracinoyl dehydromelitensin,[8] 8α-sarracinoyl salonitenolide,[8] 11,13-dihydro-onopordopicrin,[9] the lignan arctigenin 4′-*O*-glucoside,[10] and the flavonoid acacetin.[11] The molecular formulas for all compounds were determined by ^{13}C NMR, ^{13}C DEPT NMR, and MS analysis; known compounds were identified by comparison of their physical data with those reported in the literature.

Compound **1** was assigned molecular formula $C_{20}H_{28}O_8$ by ^{13}C NMR (Table 1), ^{13}C DEPT NMR, and ESIMS experiments. The ^{13}C NMR and ^{13}C DEPT NMR spectra indicated that **1** contained two CH_3, four CH_2, and three CH carbons, as well as, one hydroxymethylene, five hydroxymethyne groups, and five quaternary carbons. The features of the ^{1}H and ^{13}C NMR spectra (Table 1) suggested an eudesmane framework (δ 1.04, s, for Me-14) with oxygenated functions at C-1, C-6, C-8, and C-15. The presence of a hydroxyl group at C-1β was inferred from the double doublet at δ 3.34 (J = 12 and 4.5 Hz). A typical triplet at δ 4.02 (J = 9.5 Hz) for H-6β indicated the presence of a hydroxyl group at C-6α. An ester moiety was located at C-8α, as evidenced from the position and pattern of the ^{1}H NMR signal at δ 5.32 (m). The presence of a 4-hydroxymethacryloyl residue attached at C-8 was deduced from the signals at δ 6.29 (s) and 5.84 (s) for H-3′ and δ 4.20 (br s) for H-4′. One exocyclic methylene conjugated with a carboxylic ester (methyl group at δ 3.77, s) was easily recognizable in the two one-proton singlets at δ 6.18 and 5.87. In the ^{1}H NMR spectrum a hemiacetal proton was also evident (δ 4.99, 1H, br s). Results obtained from 1D TOCSY[12] and DQF−COSY[13] experiments established the correlations of all protons in compound **1**, showing the sequences H-1−H-9, H-15−H-1, and H-15−H-9. The signals of the ^{13}C NMR spectrum were assigned on the basis of a direct 2D ^{1}H−^{13}C experiment (HSQC).[14] The location of the 4-hydroxymethacryloyl residue, the hydroxyl groups, and the hemiacetal group were confirmed by conducting a HMBC experiment.[14,15] The signal at δ 4.99 (H-15) correlated with carbon resonances at 24.2 (C-3), 77.8 (C-6), 54.5 (C-5), and 55.3 (C-7) ppm. The HMBC experiment also indicated connections between δ 5.32 (H-8) and 167.0 (C-1′), 35.2 (C-10), and 77.8 (C-6) ppm; δ 3.34 (H-1) and 24.2 (C-3), 54.5 (C-5), and 44.6 (C-9) ppm; and δ 2.86 (H-7) and 44.6 (C-9), 124.8 (C-13), 168.0 (C-12), and 54.5 (C-5) ppm. The chemical shifts, the multiplicities of the signals and the absolute values of the coupling constants in the ^{1}H NMR spectrum were in good agreement with a *trans*-disposition of H-5/H-6, H-6/H-7, and H-7/H-8. 1D ROESY[12] measurements supported the proposed structure and allowed the relative stereochemistry at C-7, C-10, and C-5 to be established. Thus, irradiation of the proton at δ 2.86 (H-7) affected the H-5, H-9$_{ax}$, and H-1 signals; while that of the proton at δ 1.04 (Me-14) influenced the H-6, H-8, and H-4 signals. 1D ROESY experiments supported β-orientations of the isopropenoyl group at C-7, the methyl group at C-10, and the hydroxyl group at C-1, while the ester moiety at C-8 and the hemiacetal group at C-6 and C-4 had an α-orientation. Consequently, compound **1** was established as the 6α,15α-hemiacetal of carmanin.[7]

Compound **2** was found to possess a molecular mass of 410. Its ^{13}C NMR spectrum (Table 1) displayed 21 carbon signals that, by DEPT, were assigned as three CH_3, five CH_2, eight CH, and five quaternary carbon atoms, allowing for a molecular formula of $C_{21}H_{30}O_8$. Also, for this compound the features of the ^{1}H (Table 1) and ^{13}C NMR spectra suggested an eudesmane ring similar to carmanin[7] except for the acyl group. The ester moiety, located at C-8α (72.0 ppm) was deduced from the position and pattern of the H-8 signal at δ 5.45 (br dd, J = 10.0 and 12.0 Hz), and was

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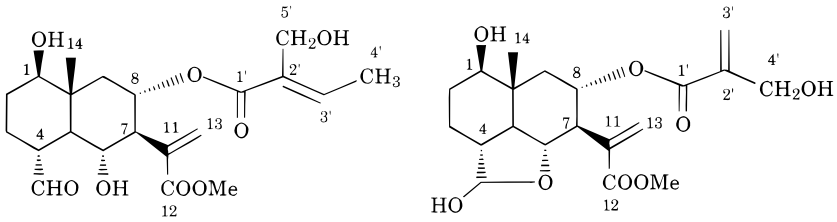
10.1021/np990098z CCC: $18.00
Published on Web 09/11/1999

Chart 1



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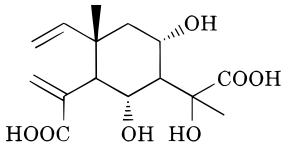

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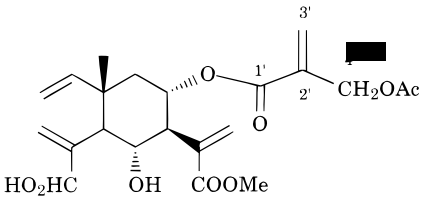

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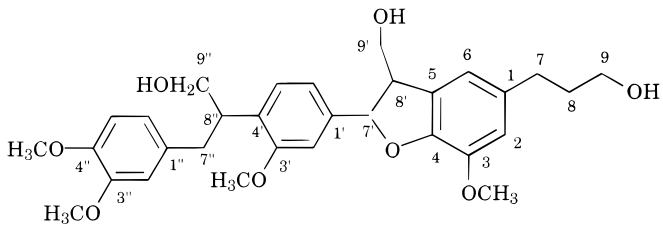

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Table 1. ^{1}H and ^{13}C NMR (600 MHz) Data for Compounds **1** and **2** (CD_3OD)[a]

	1		**2**	
position	^{1}H	^{13}C	^{1}H	^{13}C
1	3.34 dd (12.0, 4.5)	79.0	3.34 dd (11.0, 5.0)	76.0
2a	1.76 m	30.4	1.79 m	25.0
2b	1.36 m		1.58 m	
3a	1.76 m	24.3	2.41 m	28.1
3b	1.76 m		1.45 m	
4	1.90 ddd (11.0, 11.0, 3.0)	41.4	2.57 dddd (11.0, 11.0, 4.0, 3.0)	47.9
5	1.50 dd (11.0, 11.0)	54.5	2.20 dd (11.0, 11.0)	32.0
6	4.02 t (9.5)	77.8	4.03 t (9.5)	67.0
7	2.86 t	55.3	2.57 t	58.0
8	5.32 br dd (12.0, 10.0)	74.2	5.45 br dd (12.0, 10.0)	72.0
9a	2.30 dd (13.0, 4.0)	44.6	2.47 dd (13.0, 4.0)	43.0
9b	1.35 dd (13.0, 12.0)		1.26 dd (13.0, 12.0)	
10		35.2		40.7
11		136.0		138.0
12		168.0		169.0
13a	6.18 s	124.8	6.26 s	125.0
13b	5.87 s		5.73 s	
14	1.04 s	11.2	1.04 s	12.6
15	4.99 br s	107.0	9.35 d (4.0)	204.0
1′		167.0		167.0
2′		140.2		133.0
3′a	6.29 s	128.3	6.96 q (7.0)	142.2
3′b	5.84 s			
4′	4.20 br s	60.7	1.92 d (7.0)	15.0
5′			4.21 br s	58.0
OCH_3	3.77 s	51.9	3.76 s	51.9

[a] *J* values are in parentheses and reported in Hz; chemical shifts are given in δ units.

characterized by the presence of a methyl doublet at δ 1.92, which was coupled with a multiplet of a methine group (δ 6.96) and a hydroxymethyl moiety (δ 4.21, br s). The chemical shift and the pattern of this signal, according to ^{13}C NMR spectrum and HSQC results, suggested the presence of a 2-hydroxymethyl-2-butenoyl group. The structure of **2** was confirmed by a series of diagnostic HMBC correlations: H-8/C-10, H-8/C-1′; CH_3-4′/C-2′; H-5′/C-1′; H-4/C-2, H-4/C-6, H-4/C-15; H-1/C-5, H-1/C-3, H-1/C-9; H-7/C-5, H-7/C-13. Finally, the aldehyde group at C-4 was established as equatorial from features of the signal of H-4 (δ 9.35) and by comparison with literature data.[7] Thus, compound **2** was assigned as the methyl ester of 8α-(2′-hydroxymethyl-2′-butenoyloxy)-1β,6α-dihydroxy-15-oxo-11(13)-eudesmen-12-oic acid.

The NMR data of **3** showed typical signals that clearly indicated the presence of an elemane framework; particularly in its ^{1}H NMR spectrum, the signals of elemane skeleton were at δ 5.90 (H-1), 5.33 (H-3a), 5.22 (H-3b), 5.04 (H-2a), and 4.99 (H-2b), respectively.[16−18] A typical doublet at δ 2.91 for H-5 and a typical double doublet signal at δ 2.82 (1H, dd, J = 9.5 and 11.0 Hz) for H-7 indicated a *trans*-disposition of H-5/H-6, H-6/H-7, and H-7/H-8, and so the oxygenated functions at C-6 and C-8 should be α-oriented.[16,17] The main differences between the ^{13}C NMR spectrum of elemacarmanin[16] and that of compound **3** were the presence of a carboxyl signal at 175.0 ppm for **3**, instead of C-15 hydroxymethylene, and the presence of methyl signal a 13.5 ppm, instead of a C-13 methylene. Furthermore, the presence of a signal δ 1.29 (3H, d, J = 6.5 Hz), ascribable to a methyl group at C-13 showed **3** to be 11,13-dihydro-15-carboxyelemane.

Compound **4** was assigned a molecular formula of $C_{21}H_{30}O_8$ as determined by ^{13}C NMR, ^{13}C DEPT NMR, and ESIMS experiments. Compound **4** was identified as a 4′-acetyl derivative of elemacarmanin,[7,16] because its NMR spectra were similar except for the signal due to the 8-acyl side chain. Other differences were the presence of a methyl at δ 1.98 (s) in the ^{1}H NMR spectrum, signals at δ 21.0

Table 2. ^{1}H and ^{13}C NMR (600 MHz) Data for Compound **5** (CD_3OD)[a]

position	^{1}H	^{13}C
1		129.1
2	6.97 br s	113.0
3		147.0
4		145.0
5		140.0
6	6.75 br s	117.6
7	2.69 br t (7.0)	32.0
8	1.86 m (7.0)	35.0
9	3.61 t	61.0
1′		134.5
2′	6.61 d (1.5)	112.9
3′		146.5
4′		122.0
5′	6.80 d (8.0)	115.8
6′	6.85 dd (8.0, 1.5)	119.3
7′	5.52 d (7)	88.0
8′	3.50 ddd (6.0)	55.5
9′a	3.86 dd (11.0, 7.0)	64.4
9′b	3.79 dd (11.0, 5.0)	
1″		132.0
2″	6.75 br s	113.8
3″		146.7
4″		142.8
5″	6.68 d (8.0)	113.8
6″	6.56 dd (8.0, 1.5)	115.3
7″a	2.70 dd	35.0
7″b	2.69 dd	
8″	1.93	44.0
9″	3.64	61.2
OCH_3	3.76 s	55.8
	3.84 s	56.0
	3.85 s	56.0
	3.87 s	56.0

[a] *J* values are in parentheses and reported in Hz; chemical shifts are given in δ units.

(CH_3) and 168.2 (C) in the ^{13}C NMR spectrum, and the chemical shift of H_2-4′ (see Experimental Section), which was shifted downfield in **4**. This suggested that **4** was esterified at position C-4′ with an acetyl residue, so that this compound was assigned structurally as 4′-acetylelemacarmanin.

The molecular formula of compound **5** ($C_{31}H_{38}O_8$) was determined from its ESIMS, FABMS, ^{13}C NMR (Table 2), and ^{13}C DEPT data. The mass spectrum showed a very small $[M - H]^-$ peak at *m*/*z* 537, with the major peaks observed at *m*/*z* 397, 340, 322, and 310. The $[M - H]^-$ peak implied that the molecule consisted of three phenylpropanoid units. The intense peak at *m*/*z* 340 and those at *m*/*z* 322 and 310 indicated the presence of a CH_2OH group in this molecular fragment. The 600 MHz ^{1}H NMR spectrum of **5** (Table 2) exhibited the presence of 38 protons, each of which was identified from the ^{1}H−^{1}H DQF−COSY spectrum. Four signals (3H, s) for aromatic methoxyl groups resonated at δ 3.76, 3.83, 3.85, and 3.87. Signals at δ 6.97 (1H, br s), 6.85 (1H, dd J = 8.0 and 1.5 Hz), 6.80 (1H, d, J = 8.0 Hz), 6.75 (1H × 2, br s), 6.68 (1H, d, J = 8.0 Hz), 6.61 (1H, d, J = 1.5 Hz), and 6.56 (1H, dd, J = 8.0 and 1.5 Hz) suggested a structure containing two 1,3,4-trisubstituted aromatic rings and one 1,3,4,5-tetrasubstituted aromatic moiety. The doublet at δ 5.52 could be assigned to a CH adjacent to an aromatic ring and the oxygen atom of the ether linkage in a dihydrobenzofuran unit, while a doublet of doublet of doublets at δ 3.50 could be assigned to the other proton of the dihydrobenzofuran ring.[19] The assignments of all protonated carbons were accomplished by interpretation of the HSQC NMR spectrum. The DQF−COSY and 1D TOCSY spectra of **5** revealed spin systems due to three segments [(C-7″−C-9″); (C-7′−C-9′); (C-7−C-9)]. These segments were connected to aromatic rings using the HMBC spectrum: the connection with the aromatic ring A was suggested by the connectivities H-6/C-7 and H-2/C-7, while the aromatic ring B was positioned from the observation of HMBC correlations for H-7′/C-2′, H-7′/C-6′, H-7′/C-9′, H-7′/C-4, H-7′/C-1′, H-2′/C-8′, H-2′/C-6′, H-2′/C-4′. The third aromatic ring C was attached to the C-4′ position of ring B (HMBC cross-peaks: H-7″/C-4′, H-7″/C-9″, H-7″/C-2″, H-7″/C-1″; H-9″/C-4′; H-2″/C-4″, H-2″/C-6″; H-6″/C-7″, H-6″/C-8″, H-6″/C-3″). It was therefore likely that compound **5** consisted of three phenylpropanoid moieties linked together, with both terminal units being phenylpropanol derivatives; these were joined by the nonaromatic portion of a dihydrobenzofuran ring and by a C−C bridge, respectively, to the third unit, which formed the central part of the molecule. The relative orientation of the substituents at the 7′- and 8′-position were determined to be *trans* from the observation of cross-peaks between H-7′ and H-9′a, and H-8′ and H-2′ in the 1D ROESY spectrum.[20−23] Moreover, the stereochemistry of the benzofuran ring of **5** was determined by comparison of the spectral data with those of related compounds.[20−23] Furthermore, the HMBC data (Figure 1) provided additional evidence for the positions of the substituents. Therefore, compound **5** was assigned the structure 3-hydroxymethyl-5-(3-hydroxypropyl)-7-methoxy-2-{3-methoxy-4-[1-(3,4-dimethoxybenzyl)-2-hydroxyethyl]phenyl}-2,3-dihydrobenzofuran.

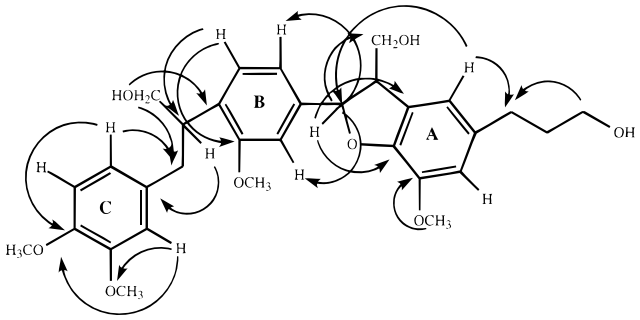

Figure 1. HMBC correlations of compound **5**.

The methanolic extract of *O. illyricum* was fractionated with H_2O and *n*-BuOH, and the latter was submitted to Sephadex LH-20 column chromatography followed by HPLC to give 5-hydroxy-3,4′-dimethoxybibenzyl-2-carboxylic acid[24] and several known flavonoids identified as acacetin 7-*O*-β-D-glucuronide, naringenin 7-*O*-neohesperidoside, and apigenin 7-*O*-β-D-glucuronide, by comparison with literature data.[25]

The present investigation on *O. illyricum* emphasizes that onopordopicrin, as well as closely related sesquiterpene lactones and hydroxyl esters, are characteristic constituents of the *Onopordum* genus. *O. illyricum*, in addition to providing 8-(4′-hydroxymethacrylate) derivatives, widespread among the previously studied *Onopordum* species, is characterized by the occurrence of 8-(5-hydroxy)tiglyloyloxy sesquiterpene lactones and hydroxyester sesquiterpene derivatives. Stilbenoid compounds were isolated for the first time in this genus, with 5-hydroxy-3,4′-dimethoxybibenzyl-2-carboxylic acid being a derivative of lunularic acid, a compound reported to have interesting biological activity as a growth inhibitor and dormancy factor.[26,27] Lunularic acid is ubiquitous in liverworts and algae, where it is considered an endogenous growth inhibi-

tor, replacing the growth regulatory function of abscisic acid of higher plants.[28]

Experimental Section

General Experimental Procedures. Optical rotations were measured on a Perkin−Elmer 241 polarimeter using a sodium lamp operating at 589 nm. UV spectra were obtained on a Perkin−Elmer Lambda 11 spectrophotometer. A Bruker DRX-600 NMR spectrometer, operating at 599.19 MHz for ^{1}H and 150.86 MHz for ^{13}C, using the UXNMR software package was used for NMR experiments; chemical shifts are expressed in δ (ppm) referring to the solvent peaks, δ_H 3.34 and δ_C 49.0 for CD_3OD. DEPT NMR experiments were performed using a transfer pulse of 135° to obtain positive signals for CH and CH_3 and negative ones for CH_2. Polarization transfer delays were adjusted to an average CH coupling of 135 Hz. ^{1}H−^{1}H DQF−COSY,[29] ^{1}H−^{13}C HSQC, and HMBC[14,15] experiments were carried out using the conventional pulse sequences as described in the literature, and 1D TOCSY[12] spectra were acquired using a waveform generator-based GAUSS-shaped pulse, at mixing times ranging from 80 to 100 ms and a MLEV-17 spin-lock field of 10 MHz preceded by a 2.5 ms trim pulse. EIMS and FABMS (negative mode) were recorded with a VG ZAB instrument; ESIMS were obtained with a Hewlett−Packward HP-1100 MSD spectrometer in the electrospray ionization negative mode. HPLC separations were performed on a Waters 590 series pumping system equipped with a Waters R401 refractive index detector and with a Waters μ-Bondapak C_{18} column and U6K injector. Si gel column chromatography was carried out with Merck Kieselgel 60 (70−230 mesh). TLC was conducting on silica 60 F_{254} gel-coated glass sheets.

Plant Material. The flowers of *O. illyricum* were collected after complete ripening of the fruits at Novara di Sicilia, Messina, Italy, in July 1997. A voucher specimen is deposited in the Herbarium of Istituto e Orto Botanico of Messina University, Italy, voucher number E34.

Extraction and Isolation. The air-dried, powdered flowers (400 g) of *O. illyricum* were defatted with *n*-hexane and successively extracted in a Soxhlet apparatus with $CHCl_3$ and $CHCl_3$−MeOH (9:1), each for 24 h, to give 18.0 and 10.0 g of residue, respectively. The plant material was then extracted at room temperature for 4 weeks with MeOH to give 8.0 g of residue, which was partitioned between *n*-BuOH and H_2O. Part of the $CHCl_3$ extract (8.0 g) was chromatographed on a Si gel column eluting with $CHCl_3$ followed by increasing concentrations of MeOH (between 1% and 50%) in $CHCl_3$ to give the pure compounds onopordopicrin,[6] 8α-sarracinoyl dehydromelitensin,[8] and acacetin[11] and 70 fractions. Fractions 45, 50, 52, 58, and 64 were submitted to reversed-phase HPLC on a C_{18} μ-Bondapak column (30 cm × 7.8 mm, flow rate 2.5 mL min^{-1}) with MeOH−H_2O (45:55) to yield, respectively, 8α-sarracinoyl salonitenolide,[8] 11,13-dihydro-onopordopicrin[9] from fraction 45; elemacarmanin,[7,16] 4-*epi*-carmanin,[7] **3** (t_R= 12 min, 11 mg), **4** (t_R= 19 min, 13 mg), and **5** (t_R= 14 min, 13 mg) from fraction 50; **2** (t_R= 14 min, 10 mg) from fraction 52; **1** (t_R= 37 min, 15 mg) and carmanin[7] from fraction 58; and arctigenin 4′-*O*-D-glucoside[10] from fraction 64. Chromatography of the *n*-BuOH extract (1 g) over a Sephadex LH-20 column eluting with MeOH gave pure 5-hydroxy-3,4′-dimethoxybibenzyl-2-carboxylic acid,[24] naringenin 7-neohesperidoside, acacetin 7-*O*-β-D-glucuronide, and apigenin 7-*O*-β-D-glucuronide.[25]

Compound 1: pale yellow oil; $C_{20}H_{28}O_8$; $[\alpha]^{25}_D$ +44° (*c* 0.05, MeOH); ^{1}H NMR and ^{13}C NMR data, see Table 1; ESIMS *m/z* 395 [M − H]$^-$, 339 [M − H − 56]$^-$, 324 [M − H − 71]$^-$, 279 [M − H − 116]$^-$; *anal.* C 60.53%, H 7.15%, O 32.32%, calcd for $C_{20}H_{28}O_8$, C 60.59%, H 7.12%, O 32.29%.

Compound 2: colorless oil; $C_{21}H_{30}O_8$; $[\alpha]^{25}_D$ +98° (*c* 0.1, MeOH); ^{1}H NMR and ^{13}C NMR data, see Table 1; EIMS *m/z* 410 [M]$^+$, 351 (55), 333 (21), 295 (100), 236 (43); *anal.* C 60.97%, H 7.61%, O 31.42%, calcd for $C_{21}H_{30}O_8$, C 61.45%, H 7.37%, O 31.18%.

Compound 3: white yellow oil; $C_{15}H_{22}O_6$; $[\alpha]^{25}_D$ +3.5° (*c* 0.05, MeOH); ^{1}H NMR δ 5.90 (1H, dd, J = 11.0, 17.5 Hz, H-1), 5.33 (1H, br s, H-3a), 5.22 (1H, br s, H-3b), 5.04 (1H, d, J = 11.0 Hz, H-2), 4.99 (1H, d, J = 17.5 Hz, H-2), 4.25 (1H, dd, J =11.5, 12.0 Hz, H-6), 3.74 (1H, m, H-8), 2.91 (1H, d, J = 11.5 Hz, H-5), 2.82 (1H, dd, J = 9.5, 11.0 Hz, H-7), 2.74 (1H, dd, J = 4.0, 12.5 Hz, H-9), 2.25 (1H, m, H-11), 2.10 (1H, dd, J = 10.0, 12.5 Hz, H-9), 1.29 (3H, d, J = 6.5 Hz, H-13), 1.22 (3H, s, H-14); ^{13}C NMR δ 175.0 (C-15), 173.0 (C-12), 146.0 (C-1), 145.5 (C-4), 114.0 (C-2), 110 (C-3), 79.6 (C-6), 69.3 (C-8), 56.0 (C-7), 48.0 (C-5), 44.5 (C-9), 44.0 (C-11), 42.0 (C-10), 15.0 (C-14), 13.5 (C-13); ESIMS *m/z* 297 [M − H]$^-$, 253 [M − H − 44]$^-$, 209 [M − H − (44+44)]$^-$; *anal.* C 60.03%, H 7.68%, O 32.29%, calcd for $C_{15}H_{22}O_6$, C 60.39%, H 7.43%, O 32.18%.

Compound 4: white yellow oil; $C_{21}H_{30}O_8$; $[\alpha]^{25}_D$ +28° (*c* 0.05, MeOH); ^{1}H NMR δ 6.30 (1H, br s, H-3′a), 6.10 (1H, br s, H-13a), 5.85 (1H, br s, H-13b), 5.81 (1H, dd, J = 11.0, 17.5 Hz, H-1), 5.77 (1H, br s, H-3′b), 5.39 (1H, br s, H-3), 5.02 (1H, br s, H-3), 4.99 (1H, d, J = 11.0 Hz, H-2), 4.95 (1H, d, J = 17.5 Hz, H-2), 5.38 (1H, m, H-8), 4.41 (1H, d, J = 11.0 Hz, H-4′a), 4.28 (1H, dd, J = 11.5, 12.0 Hz, H-6), 4.22 (1H, d, J = 11.0 Hz, H-4′b), 4.03 (1H, br s, H-15a), 3.93 (1H, br s, H-15b), 2.68 (1H, m, H-7), 1.95 (1H, d, J = 11.5 Hz, H-5), 1.75 (1H, dd, J = 4.0, 12.5 Hz, H-9a), 1.67 (1H, dd, J = 10.0, 12.5 Hz, H-9b), 1.98 (3H, s, Me), 1.22 (3H, s, H-14); ^{13}C NMR δ 175.0 (acetyl) 169.0 (C-12), 167.0 (C-1′), 147.0 (C-1), 140.5 (C-4), 138.0 (C-11), 121.3 (C-13), 113.0 (C-2), 111.0 (C-3), 72.6 (C-6), 72.3 (C-8), 56.0 (C-7), 52.0 (C-5), 44.2 (C-9), 40.0 (C-10), 21.0 (acetyl), 15.0 (C-14); ESIMS *m/z* 409 [M − H]$^-$; *anal.* C 61.03%, H 7.68%, O 31.29%, calcd for $C_{21}H_{30}O_8$, C 61.45%, H 7.37%, O 31.18%.

Compound 5: pale yellow oil; $C_{31}H_{38}O_8$; $[\alpha]^{25}_D$ +36° (*c* 0.05, MeOH); UV (MeOH) λ_{max} (log ϵ) 282 (3.46), 239 (sh) (4.15); ^{1}H NMR and ^{13}C NMR data, see Table 2; FABMS *m/z* 537 [M − H]$^-$, 397 [M − H − 140]$^-$, 340 [M − H − 197]$^-$, 322 [M − H − 215]$^-$, 310 [M − H − 227]$^-$; *anal.* C 68.52%, H 7.56%, O 23.92%, calcd for $C_{31}H_{80}O_8$, C 69.13%, H 7.11%, O 23.76%.

Acknowledgment. The authors wish to thank Dr. Ammar Bader and Dr. Rosalba Villari, Istituto ed Orto Botanico, Università di Messina, for collecting and identifying the plant material. The work was in part supported by a grant from MURST (Ministero Università e Ricerca Scientifica e Tecnologica−Roma).

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NP990098Z