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ARGUTICININ, A SESQUITERPENE FROM *PLUCHEA ARGUTA*

VIQAR UDDIN AHMAD and KANIZ FIZZA

H.E.J. Research Institute of Chemistry, University of Karachi, Karachi-32, Pakistan

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Key Word Index—*Pluchea arguta*; Compositae; sesquiterpenoid; eudesmane.

Abstract—A new eudesmane type of sesquiterpene, arguticinin was isolated from the whole plant of *Pluchea arguta* and its structure determined by spectroscopic studies.

INTRODUCTION

Pluchea arguta Boiss. (Syn. *Conyza odontophylla* Boiss.) is a weed commonly found in Sind and other parts of Pakistan [1]. In view of the medicinal properties of plants belonging to this genus [2], a chemical investigation of *P. arguta* was undertaken. Recently we have reported the isolation of two new sesquiterpenes of the eudesmane series along with some known compounds from this plant [3, 4]. In this paper we describe the isolation and structure elucidation of arguticinin (**1**) together with 4α-acetoxy-3α-(2′-methyl-2′,3′-epoxybutyryloxy)-11-hydroxy-6,7-dehydroeudesman-8-one (**2**) which was previously reported from *P. foetida* [5, 6].

RESULTS AND DISCUSSION

Arguticinin (**1**) is a colourless gum, isolated by repetitive flash column chromatography of sesquiterpenic mixture as described in the Experimental. The negative ion fast atom bombardment mass spectrum of **1** showed $(M-H)^-$ peak at *m/z* 407 while the electron impact high resolution mass spectrum gave the exact mass 408.2215 corresponding to the molecular formula $C_{22}H_{32}O_7$. The peak at *m/z* 366.2038 attributed to the formula $C_{20}H_{30}O_6$ was due to the loss of ketene (CH_2=C=O) from the the molecular ion. A fragment appeared at *m/z* 333.1705 having the composition $C_{19}H_{22}O_5$ due to the loss of CH_3 and H_2O from the fragment ion at *m/z* 366. Another fragment at *m/z* 233.1179 with the composition $C_{14}H_{17}O_3$ was due to the loss of epoxyangelate from the fragment ion *m/z* 333. The UV absorption maxima at 225 nm (log ε, 0.684), indicated the presence of a conjugated carbonyl group. The IR spectrum exhibited bands at 3400, 1745, 1730 and 1680 cm^{-1} corresponding to hydroxyl, acetate carbonyl, epoxy angelate carbonyl, and α,β-unsaturated ketone, respectively. The ^1H NMR spectrum ($CDCl_3$, 300 MHz) showed a doublet at δ6.85 characteristic of an olefinic proton (H-6). It is known that the H-6 signal is shifted downfield from δ6.85 to 7.01 when the acetate group is present at the C-4 position as in **2** [6]. This upfield shift of the H-6 value clearly indicated that the oxygen function at C-4 was in the β-position rather than the α-position. This was also confirmed by the slightly upfield shift of the acetate methyl at δ1.98 and 15-Me at δ1.38 which is characteristic for a 4β-acetoxy group. Two singlets at δ1.44 (3H) and 1.46 (3H) were due to the methyls at C-11. The characteristic signals for epoxyangelate appeared at δ3.09 as a quartet for 1H having a coupling constant 6 Hz, due to H-3′, a doublet (3H) at δ1.34 (J = 5.4 Hz) for 4′-Me and a singlet at δ1.59 integrating for 3H was assigned to 5′-Me. A triplet resonating at δ5.90 (J = 2.8 Hz) is characteristic for the geminal proton at C-3 and from this downfield shift the position of epoxyangelate ester was determined and the stereochemistry at C-3 was deduced by the coupling $J_{2,3}$ = 2.8 Hz specific for the α-orientation of the ester group.

The multiplicities of the proton signals were determined through the 2D J-resolved spectrum and coupling interactions were established by a COSY-45 experiment. The stereochemistry of the molecule at several points was established through the NOESY spectrum. Strong cross peaks were observed between H-9 and H-14. The H-9 also showed NOE interaction with H-12. The NOE interaction of H-13 at δ1.44 with the olefinic H-6 at δ6.85 and also between the H-5 and olefinic H-6 could be observed. The spatial NOE interaction between the H-15 and H-6 olefinic protons suggests the stereochemistry of 15-Me at C-4. This NOE interaction favours a β-orientation for the acetate moiety at C-4. Similarly the NOE interaction could be observed between the 3xH-5′ and H-3′ at δ1.59 and 3.09.

The ^{13}C NMR spectrum (broad band and DEPT) in $CDCl_3$ (75.4 MHz) showed that the presence of an acetyl group at C-4 (diester derivative) shifts the C-3 signal to high field but an expected strong deshielding is observed for C-4 (approximately 8 ppm from 4-*epi*-plucheinol [3]). The complete ^{13}C NMR assignments are given in Table 1.

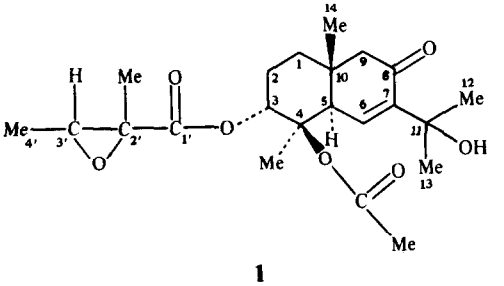

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Table 1. ^{13}C NMR chemical shifts for compound **1** ($CDCl_3$, 75.4 MHz)*

	Arguticinin (**1**)		
C	δ	C	δ
1	32.01	13	28.92
2	25.85	14	17.81
3	73.70	15	18.61
4	80.10	1′	168.20
5	49.92	2′	59.90
6	140.20	3′	59.62
7	142.29	4′	14.85
8	201.01	5′	19.25
9	57.53	OCOMe	169.23
10	38.95	OCOMe	20.25
11	72.40	—	—
12	29.41	—	—

* The status of each carbon confirmed through DEPT experiment.

Compound **2** was isolated as a colourless gum. The positive ion fast atom bombardment mass spectrum exhibited the molecular ion peak at *m/z* 408, attributable to the molecular formula $C_{22}H_{32}O_7$. The UV and IR spectra of **2** are very similar to **1**. The ^1H NMR ($CDCl_3$, 300 MHZ) spectrum is also similar to **1** but there are some differences. The olefinic proton (H-6) was observed at δ7.01 (*d*, $J = 3$ Hz). The acetate methyl resonated at δ2.01, and the stereochemistry of the acetate at C-4 followed from the chemical shift of the H-6 signal and the 15-Me signal which shifted slightly downfield as compared to **1**, i.e. at δ7.01 and δ1.54. The ^{13}C NMR values of **2** are identical to the values reported in the literature [7].

It is concluded that the isolated arguticinin (**1**) is a new diester of eudesman-11-hydroxide, which is an epimer of **2** at the C-4 position and the structure assigned is 4β-acetoxy-3α-(2′-methyl-2′3′-epoxybutyrloxy)-11-hydroxy-6,7-dehydroeudesman-8-one.

EXPERIMENTAL

The UV spectrum was measured in MeOH. The IR spectrum was determined in $CHCl_3$. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$. FABMS and HRMS were recorded on a Finigan MAT 312 double focusing mass spectrometer connected to a PDP 11/34 computer. Flash column chromatography was performed on EYELA flash CC model EF. 10. Purity of the compounds was checked on HPTLC precoated glass plates (E. Merck).

Extraction and isolation. The fresh whole plant of *Pluchea arguta* Boiss. (8 kg) was collected from Karachi and identified by the Department of Botany, University of Karachi. The plant material was soaked and homogenized in hexane, using an Ultra-turrax homogenizer and the filtrate obtained was evapd under red. pres. The residue thus obtained was chromatographed on a silica gel column with hexane, hexane–$CHCl_3$ $CHCl_3$, $CHCl_3$–EtOAc, EtOAc, EtOAc–MeOH and finally with pure MeOH. Elution with 80% $CHCl_3$–20% EtOAc afforded a fraction containing a number of closely moving sesquiterpenes. This mixture was subjected to repetitive flash CC with C_6H_6–EtOAc (6:4) as mobile phase, the first few fractions furnished pure **2** as a colourless oil, and the last fractions gave pure arguticinin (**1**) as a colourless gum. Purity of both the compounds was confirmed by HPTLC using C_6H_6–EtOAc (1:1) as developing solvent as well as on HPLC using a Z-Module with RP-18 cartridge and MeOH–H_2O (7:3) as mobile phase.

Arguticinin (**1**): Colourless oil, $[\alpha]_D^{20} + 98°$ (MeOH; *c* 0.04); UV λ_{max} (MeOH) nm (log ε): 225 (0.684); IR ν_{max} ($CHCl_3$) cm^{-1}: 3400, 1745, 1730 and 1680; ^1H NMR (300 MHz): δ1.00 (*s*, 3xH-14), 1.34 (*d*, $J = 5.4$ Hz, H-4′), 1.38 (*s*, 3x H-15), 1.44 (*s*, 3x H-13), 1.46 (*s*, 3x H-12). 1.59 (*s*, 3x H-5′), 1.98 (*s*, OCOMe), 2.37 (*m*, 2x H-9), 2.81 (*d*, $J = 3$ Hz, H-5), 3.09 (*q*, $J = 6$ Hz, H-3′), 5.90 (*t*, $J = 2.8$ Hz, H-3). 6.85 (*d*, $J = 3$ Hz, H-6). ^{13}C NMR: See Table 1; HRMS *m/z*: 408. 2215 [$C_{22}H_{32}O_7$, calcd 408.2209, M^+], 366.2038 [$C_{20}H_{30}O_6$, calcd 366.2042, M^+-(CH_2=C=O)], 351.1810 [$C_{19}H_{27}O_6$ calcd 351.1807, $M^+ - (CH_2{=}C{=}O) - Me$], 333.1705 [$C_{19}H_{25}O_5$ calcd 333.1701, $M^+ - (CH_2{=}C{=}O) - Me - H_2O$], 233. 1179 [$C_{14}H_{17}O_3$, calcd 233.1177, 333 – Epang], 215.1069 [$C_{14}H_{15}O_2$ calcd 215.1072, 333 – Epang – H_2O].

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