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Calamistrin E, the First Annonaceous Acetogenin with Double Bond in Aliphatic Chain from Genus *Uvaria*

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Abstract: Calamistrin E, the first Annonaceous acetogenin with C=C bond in the aliphatic chain from the genus *Uvaria* was isolated from *U. calamistrata*. Its structure including relative and absolute configurations was determined by chemical derivation and spectral analysis.

Keywords: Annonaceae, acetogenin, *Uvaria calamistrata*, calamistrin E.

Annonaceous acetogenins are considered as the main components with cytotoxicity in the plants of Annonaceae family. The genus *Uvaria* is one of the main plants containing Annonaceous acetogenins, and more than fifty acetogenins have been isolated from eight species of the title genus[1-5], however, acetogenins with double bond in the aliphatic chain has not yet been reported. In this paper we report the structure elucidation of calamistrin E (**1**), a new acetogenin bearing one double bond besides a tetrahydrofuran (THF) ring in the aliphatic chain. **1** indicated moderate cytotoxicity against human tumor cell lines in MTT test.

Calamistrin E (**1**) was isolated from the roots of *Uvaria calamistrata* Hance as a white waxy solid, m.p. 35.3°C; $[\alpha]_D^{19}$ +25.7 (c 0.07, MeOH). The test of **1** with Kedde reagent was positive. Its molecular formula $C_{37}H_{66}O_6$ was deduced from its FABMS (*m/z* 607 $[MH]^+$) and element analysis (found C 73.10, H 10.77; required C 73.27, H 10.89). The existence of a γ-methyl α,β-unsaturated γ-lactone was suggested by IR carbonyl absorption bands at 1763, 1739 cm^{-1}, an UV band at λ_{max} 204 nm, ^1H NMR signals at δ 7.04 (1H, d, J=1.3 Hz, H-35), 5.07 (1H, dq, J=6.8, 1.3 Hz, H-36), 2.36 (1H, m, H-3a) 2.44 (1H, m, H-3b), and 1.41 (3H, d, J=6.8 Hz, H-37), and ^{13}C NMR signals at δ 173.80 (C-1), 149.38 (C-35), 134.10 (C-2), 77.25 (C-36), 21.52 (C-3) and 19.15 (C-37). The signals at δ_C 70.91 (C-5) and δ_H 3.59 (1H, m, H-5) as well as the NMR data of the lactone moiety also indicated the presence of a 5-OH group[2]. The mono-THF ring moiety with flanking OH groups at both sides was deduced by the signals at δ 3.82 (2H, m, H-16, 19), 3.44 (2H, m, H-15, 20) in the ^1H NMR spectrum and the resonances at δ 82.63 (C-19), 82.69 (C-16), 74.07 (C-20), 74.80 (C-15) in the ^{13}C NMR spectrum. These signals also suggested that the THF moiety with flanking OH groups had a *threo-trans-threo* relative configuration on the basis of comparison with a model mono-THF ring

acetogenins[2]. The position of the THF ring (C-16 to C-19), and two flanking OH groups at C-15 and C-20 were elucidated by the diagnostic fragment ion peaks in the EIMS of **1** and its TMSi derivative (**1a**). The presence of a double bond in **1** was shown by NMR signals at δ_H 5.39 (1H, dt, J=12.5, 5.6 Hz, H-23) and 5.35 (1H, dt, J=12.5, 5.6 Hz, H-24) and at δ_C 128.79 and 130.60. The *cis* configuration of the double bond in the aliphatic chain was indicated by measurement of the vicinal coupling constant (J=12.5 Hz) between the olefinic protons in ^{1}H NMR spectrum[6]. In fact, the double bonds in the aliphatic chain of Annonaceous acetogenins found in other genera all possessed *cis* configuration. The location of the double bond between C-23 and C-24 was shown by the fragment ion peak (*m/z* 181) in the EIMS of **1** and **1a** (see **Figure 1**). The resonance at δ 28.67 (C-22) in the ^{13}C NMR spectrum supported the location of the double bond[2].

The absolute configurations of carbinol chiral centers in 1 were determined by the advanced MTPA ester method2. According to the 1H NMR data analysis of the diagnostic protons of its (R)- and (S)-tri-MTPA esters (1r, 1s) (see Table 1), C-5, C-15 C-16, C-19 and C-20 in 1 were determined as 5R, 15R, 16R, 19R and 20R respectively. The absolute configuration of C-36 was directly assigned as S[2].

Figure 1. The diagnostic fragment ions from the EIMS of **1** and **1a**

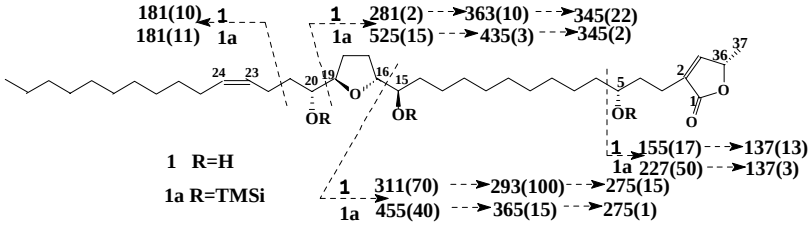

Table 1. The ^{1}H NMR data of the diagnostic protons of **1r** and **1s** (in $CDCl_3$)

H	3	5	6	14	15	16	19	20	35	36	37	23-24
δ_S	2.38	4.87	1.59	1.51	5.27	4.10	3.88	5.07	6.95	4.97	1.39	5.38
δ_R	2.41	4.88	1.58	1.48	5.26	4.11	3.87	5.10	7.03	4.98	1.40	5.33
$\Delta\delta$ (S-R)	-	-	+	+	+	-	+	-	-	-	-	+

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