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A NON-OXIDIZED MELAMPOLIDE AND OTHER GERMACRANOLIDES FROM *ARISTOLOCHIA YUNNANENSIS**

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Key Word Index—*Aristolochia yunnanensis*; Aristolochiaceae; melampolide; germacranolides; sesquiterpenes.

Abstract—Four sesquiterpene lactones have been isolated from the underground parts of *Aristolochia yunnanensis* growing in the Yunnan province of China. Three were identified as the known germacranolides costunolide, dehydrocostuslactone and α-cyclocostunolide. The structure of the fourth compound, the non-oxidized melampolide, was elucidated by spectroscopic methods and X-ray analysis.

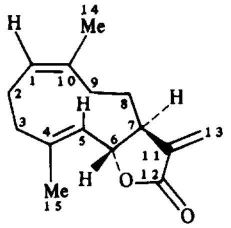
INTRODUCTION

Aristolochia yunnanensis (Aristolochiaceae), in Chinese 'Yunnan Ma Don Ling', a perennial climber, growing in the Yunnan province (China), is used in traditional medicine (drug name 'Nan Mu Xiang') to treat gastrointestinal diseases, trichomoniasis and various pain conditions [1, 2].

Upon petrol–ether (1 : 1) extraction of the underground parts of *A. yunnanensis* following the usual procedure, a neutral fraction has been obtained, from which four sesquiterpene lactones could be isolated by CC. Three of them have been identified as costunolide (**1**) [3], dehydrocostuslactone [4] and α-cyclocostunolide [5] from their physical and spectroscopical properties.

RESULTS AND DISCUSSION

The fourth sesquiterpene lactone **2** ($\tilde{\nu} = 1762\ \mathrm{cm}^{-1}$) has the same molecular formula ($C_{15}H_{20}O_2$) and similar spectroscopic data as **1**, which suggests a similar structure. Differences however, exist in mp, optical rotation and NMR data (Tables 1 and 2). In the ^{1}H NMR the olefinic proton signal at δ5.05 shows a vicinal coupling to the signal at δ4.57 ($J = 10.5$ Hz) and an allylic coupling to δ1.81 ($J = 1.5$ Hz) and can therefore be assigned to H-5 (Table 1). Hence, the methyl signal of δ1.81 corresponds to C-15 and the signal at δ1.68 to the C-14 methyl group. The ^{13}C NMR shift values of both methyl groups were identified with the aid of C,H correlation (Table 2) as δ17.23 for C-15 and δ21.91 for C-14. As the shift value of the methyl carbon C-14 is over 20 ppm, we conclude, that the 1(10) double bond should be *cis*-configurated, according to the rule of Lange and Galatsis [6]. Therefore **2**



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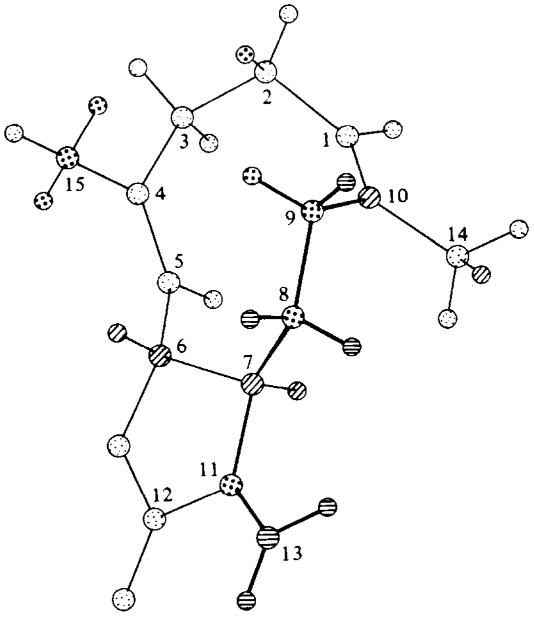

Fig. 1. Molecular structure of melampolide (**2**).

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*Dedicated to Prof. Dr F. Zymalkowski (Bonn) in honour of his 75th birthday.

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Table 1. ^{1}H NMR spectral data of compounds **2** and **1** (300 MHz, $CDCl_3$)

H	**2**	H, H-COSY correlated with H	**1**
1	5.16 *tq*, 1H	2, 2′, 14	4.84 *br dd*, 1H
2	1.76–2.1 *m*, 5H	1	1.67 *qd*, 1H
2′	—	—	2.0–2.4 *m*, 6H
3	1.76–2.1 *m*, 5H	—	2.0–2.4 *m*, 6H
3′	2.14 *m*, 1H	—	2.44 *dd*, 1H
5	5.05 *dd*, 1H	6, 15	4.73 *brd*, 1H
6	4.57 *dd*, 1H	5, 7	4.57 *t*, 1H
7	2.48 *ddq*, 1H	6, 8, 13, 13′	2.56 *t*, 1H
8	1.50 *dddd*, 1H	7, 8′, 9, 9′	2.0–2.4 *m*, 6H
8′	2.27 *dddd*,	8	—
9/9′	1.76–2.1 *m*, 5H	8	2.0–2.4 *m*, 6H
13	5.41 *d*, 1H	7	5.51 *d*, 1H
13′	6.14 *d*, 1H	7	6.26 *d*, 1H
14	1.68 *d*, 3H	1	1.40 *s*, 3H
15	1.81 *d*, 3H	5	1.70 *s*, 3H

J (Hz) compound **2**: 1, 2 = 1, 2′ = 8.5; 1,14 = 1.5; 5,6 = 10.5; 5,15 = 1.5; 6,7 = 9.5; 7,8 = 12; 7,13 = 3.3; 7,13′ = 3.5; 8,8′ = 14; 8,9 = 5; 8,9′ = 2.5; 8′,9 = 13; 8′9′ = 6.5; 8′,7 = 3.8.

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

C	**2**	DEPT	HETCOR correlated with	**1**
1	124.87	CH	H-1	127.01
2	26.71	CH_2	$\delta = 2$; 1.8	28.18
3	38.87	CH_2	H-3′; δ 1.8	41.11
4	138.13	C	—	140.04
5	124.45	CH	H-5	127.23
6	80.66	CH	H-6	81.95
7	44.98	CH	H-7	50.50
8	25.41	CH_2	H-8, 8′	26.33
9	25.08	CH_2	δ 1.9	39.56
10	136.73	C	—	136.93
11	140.10	C	—	141.44
12	170.31	C	—	170.37
13	118.39	CH_2	H-13, 13′	119.65
14	21.91	Me	14-Me	16.28
15	17.23	Me	15-Me	17.51

posesses a melampolide structure. This is confirmed by the coupling constants $J_{6,7} = 9.5$ Hz and $J_{7,13} = 3.5$ and 3.3 Hz, respectively, as well as by $J_{1,2}$ and $J_{1,2'}$, being twice as large as in **1** (Table 1). Consequently, **2** represents the hitherto unknown, non-oxygenated melampolide. The structure was additionally confirmed by X-ray analysis (Fig. 1).

EXPERIMENTAL

Mp: uncorr. TLC on silica gel F_{254}, 0.25 mm (Merck). CC on silica gel 60, 230–400 mesh (Merck).

Plant material, extraction and isolation. Dried underground parts of *A. yunnanensis* Franch. were obtained from the market (Fa. China-Kräuter, Ahrensburg, F. R. G.) and identified according to ref. [2].

Dried powdered material was extracted at room temp. ×4 with petrol–Et_2O (1:1). After evapn and soln of the residue in Et_2O, acids were removed by extraction with 5% Na_2CO_3 soln. The remaining neutral fr was sepd by CC (CH_2Cl_2). Frs of this sepn with R_f 0.45–0.55 (petrol–EtOAc 9:1) were again sepd by CC with petrol–EtOAc (9:1). Frs of this sepn with R_f 0.55 afforded 80 mg α-cyclocostunolid and with R_f 0.47 1.36 g dehydrocostuslacton.

Frs of the CH_2Cl_2 sepn with R_f 0.40–0.46 (petrol–EtOAc 17:3) were again sepd by CC with petrol–EtOAc (17:3). Frs from this sepn with R_f 0.41 gave 1.5 g **1**, with R_f 0.46 and 0.17 g **2**.

Melampolide [1 (10)-cis-*costunolide*] (**2**). Colourless plates, mp 144–145° (Et_2O); $[\alpha]_D^{20} + 1.4°$ ($CHCl_3$; *c* 0.84). ν_{max}^{KBr} cm^{-1}: 3030 (w), 2962 (m), 2920 (m), 2862 (m), 2844 (m), 1762 (vs), 1667 (w), 1440 (m), 1410 (m), 1380 (m), 1322 (m), 1303 (m), 1260 (s), 1248 (m), 1152 (s), 1007 (w), 977 (s), 960 (m), 935 (s), 870 (w), 847 (m), 812 (m), 796 (w), 700 (w), cm^{-1}. ^{1}H NMR ($CDCl_3$): Table 1. ^{13}C NMR ($CDCl_3$): Table 2. MS (EI, 70 eV), *m/z* (%): 232 (48, $[M]^+$), 217 (26), 204 (8), 199 (5), 190 (8), 189 (7), 187 (7), 177 (9), 175 (8), 173 (6), 171 (7), 163 (7), 151 (14), 150 (17), 131 (20), 123 (50), 121 (39), 109 (54), 91 (84), 81 (100), 79 (50), 61 (25), 55 (40), 53 (75), 41 (50).

Crystal data. Compound **2** crystallized in monoclinic form with lattice parameters: $c = 14.2861(5)$, $b = 6.7489(3)$, $a = 7.070(3)$, $\beta = 102.20\,(3)°$ in the space group $P2_1$. The cell vol. was calcd as 666.246 Å^3, the number of formula units in the elementary cell amounted to $Z = 2$, so that the density was computed to be 1.16 g/cm^3. In the region $0° < 2\delta < 50°$ 5146 reflections (4647 independent reflections) were measured (graphite monochromatized MoK_α-radiation: 0.7107 Å) on an automatic four-circle diffractometer (Nicolet $P2_1$). After correcting (Lorentz and polarization effects) 2217 structure factors were used for structure determination. The structure was solved by Direct Methods (SHELXTL) using block matrix least squares calculations (non-H atoms isotropically). After the final refinement (234 parameters), the *R* value converged to 0.035 ($R_w = 0.036$ with $W = 1/\sigma^2$). Scattering factors were used for uncharged atoms (International Tables). Full crystal data of **2** are deposited at the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge, C82 1EW, UK.

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