Phytochemistry, 1980, Vol. 19, pp. 2204–2205. © Pergamon Press Ltd. Printed in England.

0031-9422/80/1001-2204 $02.00/0

A PSEUDOGUAIANOLIDE FROM *HYMENOXYS LINEARIFOLIA*

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(*Received* 21 *December* 1979)

Key Word Index—*Hymenoxys linearifolia*; Compositae; pseudoguaianolide.

Hymenoxys linearifolia Hook (tribe Heliantheae) has been investigated previously [1] and the pseudoguaianolides linearifolin-A and B, together with the flavone hymenoxin, were isolated. The same species collected near Monterrey has now been reinvestigated.

The polar fractions of the aerial parts afforded a crystalline compound which had the composition $C_{22}H_{28}O_7$. The spectral data showed that it was a methylenelactone, which contained a conjugated keto group, most probably in the five-membered ring of a pseudoguaianolide (^{1}H NMR, *dd*, δ 7.61 and 6.10). An IR band at 1740 cm^{-1} indicated that we were not dealing with a five-membered methylene lactone. Furthermore, the NMR signals of the methylene protons showed unusually small couplings. From the ^{1}H NMR spectrum it was apparent that the lactone had an acetate group (*s*, 2.05) and a 2-methylbutyric acid ester residue (*tq*, 2.32, *ddq*, 1.61 and 1.43, *t*, 0.88 and *d*, 1.08). From the same plant linearifolin-B (**1**) was isolated [1] which has NMR signals very similar to those of the new lactone. In particular, the pattern of the coupling of the low-field signals was more or less the same. However, one of these signals was located at much higher field in the spectrum of **1**, and this was assigned to the proton at C-8 bearing the free hydroxyl. Therefore this hydroxyl must be esterified in the new lactone. Furthermore, linearifolin-B has a different ester residue. However, the close similarity of the two NMR spectra strongly indicated that the new lactone was most probably a six-membered lactone with the same stereochemistry as that of **1**. The relative position of the two ester groups was established by mild saponification following the method of Herz [2]. The monoester obtained showed, by ^{1}H NMR spectroscopy, that the acetate was absent, while the methylbutyric acid ester was unchanged. Moreover, the spectrum showed that the six-membered lactone was transformed to a five-membered one and that methanol had added to the conjugated 2,3-double bond (Table 1). Most probably after hydrolysis of the acetate group at C-8, trans-esterification occurs and the isolated product has a free hydroxyl at C-9. Similar observations were made with **1**, which was transformed under very mild conditions into linearifolin-A [1].

Intensive double resonance experiments confirm the structure and stereochemistry of the new lactone as **2**, while the saponification product must be **4**. Irradiation of the ^{1}H NMR signal at δ 3.20 changed the signals at 2.41 (*dq* → *q*), 7.61 (*dd* → *d*) and 6.10 (*dd* → *d*). Therefore the *ddd* at 3.20 must be assigned to the 1α-H and the *ddq* at 2.41 to 10β-H. Irradiation of the broad singlet at 3.47 changed the signals of the 13-H and also those at 5.25 and 5.44, clearly indicating that we were dealing with the signal of the 7α-H. The same irradiation also sharpened the signal of the 9-H. Models show that we can expect a *W*-coupling. Irradiation of the 10β-H changed the signals of the 1α-H (*ddd*, 3.20) and 14-H (*d*, 1.40). The large coupling ($J_{1,10}$ = 13 Hz) further established the given configurations at C-1 and C-10. The transformation of **2** to **4** was accompanied by a change in the conformation as several couplings were altered. These changes were consistent with models. The oxygen function at C-6 in **4** probably is equatorial and the *O*-methyl group is in the β position. In

Table 1. ^{1}H NMR spectral data of compounds **2** and **4** (270 MHz, $CDCl_3$, TMS as internal standard)

	2	**4**
1-H	3.20 *ddd*	2.43 *m*
2-H	7.61 *dd*	4.02 *dd*
3-H	6.10 *dd*	2.68 *d* 2.18 *dd*
6α-H	5.25 *d*	5.16 *d*
7α-H	3.47 *s*(*br*)	3.57 *m*
8α-H	5.44 *d*(*br*)	4.96 *dd*
9α-H	4.65 *s*(*br*)	3.57 *m*
10β-H	2.41 *dq*(*br*)	2.25 *dq*
13-H	6.78 *dd*	6.44 *d*
13′-H	6.06 *dd*	6.15 *d*
14-H	1.40 *d*	1.28 *d*
15-H	1.04 *s*	0.99 *s*
2′-H	2.32 *ddq*	2.20 *ddq*
$3'_1$-H	1.01 *ddq*	1.60 *ddq*
$3'_2$-H	1.43 *ddq*	1.40 *ddq*
4′-H	0.88 *t*	0.88 *t*
5′-H	1.08 *d*	1.07 *d*
OAc	2.05 *s*	

J (Hz): **2**: 1,2 = 1.5; 1,3 = 3; 1,10 = 13; 2,3 = 6; 6β,7α = 3.7; 7α,8α ~ 1.5; 7α,13 ~ 1; 7α,13′ ~ 1; 7α,9α ~ 1; 8α,9α ~ 1.5; 9α,10β ~ 1.5; 10β,14 = 7; 13,13′ ~ 1; $2',3'_1 = 2',3'_2 = 2',5' = 3',4'$ = 7; $3'_1,3'_2$ = 13; **4**: 1,2 = 5; 2,3 = 6; 3,3′ = 19; 7,8 = 8; 7,13 = 2.5; 7,13′ = 2.2; 8,9 = 2; 10,14 = 7.

this case $J_{2\alpha,3\beta}$ should be nearly zero (angle *ca* 90°). Irradiation at 3.57 changed the signals at 5.16, 4.96, 6.44 and 6.15. Therefore the multiplet at 3.57 must be assigned to 7α-H. The $J_{6,7}$ value now was 8 Hz, which was in agreement with the proposed conformation. The angle between 7- and 8-H now is nearly 0°.

The new lactone is closely related to linearifolin-B (**1**), which, however, has not been isolated from our material. We propose the new name linearifolane (**7**) for the compound without any double bond or function. Linearifolin-B (**1**) then will be 4-oxo-6α-tiglinoyloxylinearifol-2,11 (13)-dien-8β-ol and **2** is 4-oxo-6α-(2-methylbutyryloxy)-linearifol-2,11 (13)-dien-8β-yl acetate. The roots afforded only the known acetylenes **5** and **6** [3].

EXPERIMENTAL

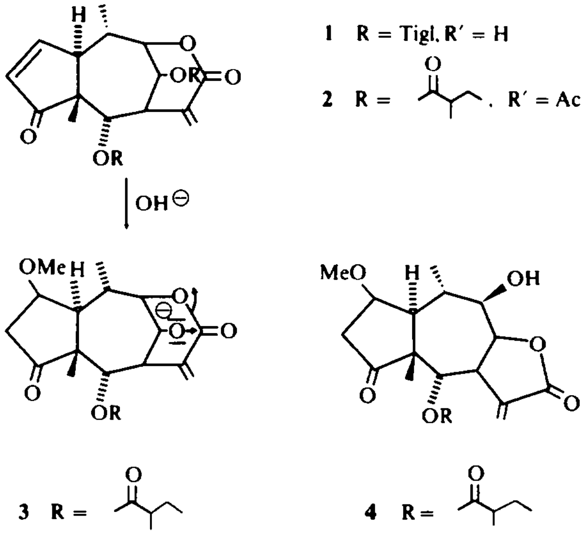
IR: CCl_4; ^1H NMR (270 MHz): TMS as int. standard; MS: 70 eV; optical rotation: $CHCl_3$. The aerial parts (2330 g) (voucher 7684) were extracted with petrol. CC (Si gel) afforded 2 g **2** (Et_2O). 100 g of roots extracted with petrol *i*-Pr_2O (1:2) yielded on CC and TLC 1 mg **5** and 2 mg **6**.

4-Oxo-6α-[2-methylbutyryloxy]-linearifol-2, 11(13)-dien-8β-ol acetate (**2**). Colourless crystals from Et_2O– petrol, mp 140°. IR ν_{max} cm^{-1}. 1740, 1725, 1630, 1585, 1465, 1390, 1370, 1230, 1150; MS *m/e* (rel. int.): 404.1835 (M^+, 2) ($C_{22}H_{28}O_7$); 344 (M − HOAc, 26); 302 (−$C_4H_9CO_2H$, 5); 260 (302 − ketene, 51); 242 (302 − HOAc, 15); 227 (242 − Me, 6); 85 ($C_4H_9CO^+$, 47); 57 (85 − CO, 100); 43 ($MeCO^+$, 46).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{\begin{array}{cccc} 589 & 578 & 546 & 436\,\text{nm} \end{array}}{\begin{array}{cccc} -81.4 & -86.1 & -102.1 & -230.2 \end{array}} \quad (c = 4.0,\ CHCl_3).$$

12 mg **2** were stirred for 8 hr with 2.4 ml 0.033 N $KHCO_3$ soln ($MeOH$–H_2O, 4:1). After evapn the residue was dissolved in CH_2Cl_2 and purified by TLC (Et_2O). Together with other products, 3 mg **4** was obtained, colourless gum; ^1H NMR, see Table 1.

Acknowledgement—We thank Dr. M. Johnston Department of Botany, University of Texas, for identification of the plant material.



1 R = Tigl, R′ = H

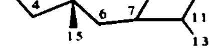
2 R = , R′ = Ac

3 R =

4 R =

$$R-CH=CH[C\equiv C]_2[CH=CH]_2(CH_2)_4CH=CH_2$$

5 R = CHO **6** R = CH_2OH



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