SECO-MANOOL AND OTHER CONSTITUENTS FROM *FLEISCHMANNIA MICROSTEMON*

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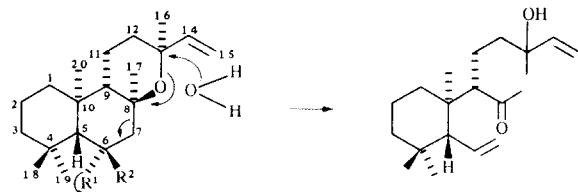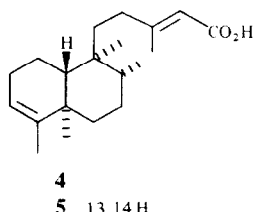
Abstract—The aerial parts of *Fleischmannia microstemon* afforded in addition to sesamin and two clerodanes, *ent*-manoyl oxide and two derivatives of the latter, one a 6β-acetoxy derivative and the other a *seco*-labdane. From *F. pratensis* and *F. gracilenta* sesamin and a clerodane, respectively, were isolated. The structures of the two diterpenes were elucidated by high field ^{1}H NMR techniques.

From the genus *Fleischmannia* (Compositae, tribe Eupatorieae), placed together with *Sartorina* in the subtribe Fleischmanniinae [1] several species have been investigated chemically [2–4]. In addition to widespread prenylated *p*-hydroxyacetophenone derivatives [2], sesamin and related lignanes [2, 4], coumarins [2], clerodanes [3], labdanes [2, 4] and caryophyllene derivatives [2, 4] have been reported. We have studied now the constituents of *F. microstemon* (Cass.) K. et R. In addition to a complex mixture of unidentified triterpenes, manoyloxide (1), the 6α-acetoxy derivative 2, the *seco*-labdane 3, the clerodanes 4 [3] and 5 [3], as well as sesamin, were isolated.

The structure of the acetate 2 followed from its ^{1}H NMR spectrum in deuteriobenzene where most signals could be assigned by spin decoupling (Table 1). As the spectrum was similar to that of manoyloxide the presence of 6-acetoxymanoyloxide was indicated. The stereochemistry followed from the observed NOE's.

Clear effects were obtained between H-18, H-5 and H-6, between H-19 and H-20, between H-20 and H-17 as well as between H-17, H-7β, H-14, H-15t and H-20. As in similar cases with an axial methyl group at C-13 the H-14 signal showed no *W*-coupling while in epimers such a coupling was always observed. Reduction of 2 followed by oxidation of the alcohol obtained gave the ketone 2a which showed a positive Cotton-effect. Therefore, most

Table 1. ^{1}H NMR spectral data of compounds 2 and 3 (400 MHz, CDCl$_3$, δ-values)

H	2	C$_6$D$_6$	3†
1β	*	0.85 *ddd*	*
1α	*	1.65 *m*	*
2β	*	1.37 *br d*	*
2α	*	1.65 *m*	*
3β	*	1.09 *ddd*	*
3α	*	1.30 *br d*	*
5	1.10 *d*	0.85 *d*	1.79 *d*
6	5.50 *ddd*	5.66 *ddd*	6.73 *ddd*
7β	1.64 *dd*	1.51 *dd*	5.17 *dd* (*c*)
7α	2.10 *dd*	2.15 *dd*	4.92 *dd* (*t*)
14	5.93 *dd*	5.99 *dd*	5.83 *dd*
15c	5.03 *dd*	5.08 *dd*	5.05 *dd*
15t	5.22 *dd*	5.39 *dd*	5.18 *dd*
16	} 1.28 *s*	1.29 *s*	1.23 *s*
17		1.31 *s*	2.11 *s*
18	0.96 *s*	1.02 *s*	0.81 *s*
19	0.94 *s*	0.96 *s*	0.90 *s*
20	1.15 *s*	1.18 *s*	0.98 *s*
OAc	2.04 *s*	1.69 *s*	

*Obscured multiplets.
† H-9 2.64 *dd*.

J[Hz]: Compound 2: 1α,1β = 1β,2α = 2α,2β = 2β,3β = 3α,3β = 13; 1β,2β = 2β,3β = 3.5; 5,6 = 2.5; 6,7β = 4; 6,7α = 2.5; 7α,7β = 14; 14,15c = 11; 14,15t = 17; 15c,15t = 1; compound 3: 5,6 = 6,7c = 10.5; 6,7t = 17; 7c,7t = 2; 9,11 = 3; 9,11′ = 11; 14,15c = 10.5; 14,15t = 17; 15c, 15t = 1.5.

1 R^1 = R^2 = H
2 R^1 = OAc, R^2 = H
2a R^1,R^2 = O

3

4

5 13,14 H

likely an *ent*-labdane was present as the octant rule should be valid [5].

The ^{1}H NMR spectrum of 3 (Table 1) clearly indicated the presence of a methyl ketone and of two vinyl groups, one with an adjacent proton and the other with a neighbouring hydroxy group as followed from the chemical shifts. Partly similar signals were observed in a *seco*-labdane with a changed side chain and a 18-hydroxy group isolated from a *Koanophyllon* species [6]. Spin decoupling allowed the assignment of most signals. All data agreed with the presence of a *seco*-manool which probably was formed by fragmentation of 2 as shown in Scheme 1. Accordingly, the most likely stereochemistry was that of the acetate 2.

A further species from Costa Rica, *F. pratensis* (Klatt.) K. et R., only gave simple sesquiterpene hydrocarbons, triterpenes and again sesamin (Experimental) while *F. gracilenta* (B. L. Robins.) K. et R., collected in Peru, afforded the clerodane 5 and taraxasteryl acetate.

So far the overall picture of the chemistry of the genus *Fleischmannia* is not very homogeneous. However, sesamin-like lignanes and diterpenes are most widespread.

EXPERIMENTAL

The air-dried aerial parts of *F. microstemon* (800 g, collected in El General, Costa Rica, voucher 116209 C.R., deposited in the Herbarium of the University of Costa Rica) was extracted with MeOH–Et$_2$O–petrol (1:1:1). The extract was separated first by CC (silica gel) and the fractions were combined into three groups (Fr. 1: Et$_2$O–petrol, 1:3; Fr. 2: Et$_2$O–petrol, 1:1 and Fr. 3: Et$_2$O and Et$_2$O–MeOH, 9:1). TLC of fraction 1 (Et$_2$O–petrol, 8.5:1.5) gave 55 mg manoyloxide, 500 mg of a triterpene mixture and 21 mg 4. Repeated CC of fraction 2 gave 140 mg 4, 200 mg 5 and two mixtures (Fr. 2/1 and Fr. 2/2). Fraction 2/1 gave by TLC (Et$_2$O–petrol, 2:3) 300 mg sesamin and 100 mg 5. TLC of fraction 2/2 (Et$_2$O–petrol, 1:1) gave 55 mg 3 (R_f 0.22) while TLC of fraction 3 (Et$_2$O) gave 440 mg 2 (R_f 0.17).

The extract of 700 g aerial parts of *F. pratensis* (collected in February 1984 in Tilaran, Costa Rica, voucher 102906 C.R.) gave by CC and TLC *ca* 20 mg each of germacrene D, caryophyllene, α-humulene, α-curcumene, caryophyllenepoxide and 50 mg sesamin.

The aerial parts of *F. gracilenta* (150 g, collected in Peru, voucher RMK 9190) gave by CC and TLC 28 mg germacrene D, 12 mg caryophyllene, 24 mg taraxasteryl acetate and 680 mg 5. Known compounds were identified by comparing the 400 MHz ^{1}H NMR spectra with those of authentic material.

6α-Acetoxy-ent-*manoyloxide* (2). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1735 (OAc); MS *m/z* (rel. int.): 348.266 [M]$^+$ (3) (calc. for C$_{22}$H$_{36}$O$_3$: 348.266), 333 [M − Me]$^+$ (2), 306 [M − ketene]$^+$ (1.5), 288 [M − HOAc]$^+$ (30), 69 [C$_5$H$_9$]$^+$ (100); [α]$_D^{24°}$ −7 (CHCl$_3$; *c* 0.4). Compound 2 (50 mg) in 5 ml Et$_2$O was reduced with 20 mg LiAlH$_4$. The alcohol obtained was stirred in CH$_2$Cl$_2$ with 50 mg PCC for 3 hr. TLC (Et$_2$O–petrol, 1:3) gave 20 mg 2a; colourless crystals, mp 118°; MS *m/z* (rel. int): 304.240 [M]$^+$ (37) (calc. for C$_{20}$H$_{32}$O$_2$: 304.240), 289 (46), 219 (38), 151 (76), 123 (78), 109 (100), 95 (96), 83 (97), 71 (86), 69 (76); ^{1}H NMR (CDCl$_3$): δ2.21 (*br s*, H-5), 2.45 (*d*, H-7), 2.63 (*br d*, H-7β), 5.94 (*dd*, H-14), 5.23 (*dd*, H-15t), 5.06 (*dd*, H-15c), 1.31 (*s*, H-16), 1.19 (*s*, H-17), 1.16 (*s*, H-18), 0.93 (*s*, H-19), 0.78 (*s*, H-20); CD (MeCN): Δε$_{315}$ + 0.50, Δε$_{303}$ + 0.82, Δε$_{296}$ + 0.86.

seco-Manool (3). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1750 (C=O); MS *m/z* (rel. int.): 306.256 [M]$^+$ (4.5) (calc. for C$_{20}$H$_{34}$O$_2$: 306.256), 288 [M − H$_2$O]$^+$ (3), 273 [288 − Me]$^+$ (6), 245 [288 − COMe]$^+$ (11), 907 [M − CH$_2$CH$_2$C(OH) (Me)CH=CH$_2$]$^+$ (10), 69 [C$_5$H$_9$]$^+$ (100); [α]$_D^{24°}$ − 15 (CHCl$_3$; *c* 1.21).

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