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NEW SESQUITERPENE LACTONES AND OTHER CONSTITUENTS FROM *FITCHIA SPECIOSA**

FERDINAND BOHLMANN,† CHRISTA ZDERO,† ROBERT M. KING‡ and HAROLD ROBINSON‡

† Institute for Organic Chemistry, Technical University, D-1000 Berlin 12, Straße des 17. Juni 135, W. Germany;
‡ Smithsonian Institution, Washington, DC 20560, U.S.A.

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Key Word Index—*Fitchia speciosa*; Compositae; sesquiterpene lactones; germacranolides; guaianolides; eudesmanes; acetylenes; isoeugenol derivatives; p-hydroxyacetophenone derivatives.

Abstract—The investigation of *Fitchia speciosa* afforded, in addition to known compounds, three new sesquiterpene lactones, iso-β-costal, two *p*-hydroxyacetophenone derivatives and an isoeugenol derivative. The structures were elucidated by spectroscopic methods. The chemotaxonomic situation in this complicated genus is discussed.

INTRODUCTION

Fitchia is a genus of six species, which only grow on some Pacific Islands. Its position in the Compositae is still a problem. Most authors regard it as an old relictual member, most probably of the tribe Heliantheae [1–3], although some more specialized features are present [4]. While some authors have placed *Fitchia* in a separate tribe, more recently this genus has been placed near the Coreopsidinae as subtribe Fitchiinae in the Heliantheae [3].

So far no chemical data are available on *Fitchia*. We therefore have investigated *F. speciosa* Cheesman to find out whether the chemistry may give indications concerning its systematic position. In addition to known compounds, three new sesquiterpene lactones, an isomer of β-costal and a new isoeugenol derivative have been isolated.

RESULTS AND DISCUSSION

The main constituent of the leaves, present in very high concentration, is dehydrocostuslactone (**7**) [5]. In addition four further lactones, which could only be separated partly, were isolated in minute amounts: the known zaluzanin-C-ester **8** [6], the corresponding 2-methylbutyrate **9**, as can be seen from the ^{1}H NMR spectrum (see Table 1) and the germacranolides **10** and **11**. Again the ^{1}H NMR data (see Table 1) are very similar to those of the known isovalerate [7], except for the signals of the ester residues. The nature of the ester groups could easily be established from the corresponding signals in the spectra of **10** and **11** (see Table 1).

The stems contain **2** and small amounts of **7**. Furthermore **1**, **4**, and **5** are present. The roots again afforded **7** as the main constituent, while the costic acid isomers are replaced by the aldehyde **3** and an isomer, which could not be separated completely from **3**. The spectral data show that this is probably the aldehyde **6**. The signals of the vinylic protons at C-15 are replaced by an olefinic methyl signal. As no new olefinic signal can be recognized a 4,5-double bond must be present.

Furthermore the roots contain the tetraynes **12–14**, germacrene A (**17**) and the isoeugenol derivative **16** together with the corresponding 2-methylbutyrate **15**, not isolated before. Its structure clearly follows from the ^{1}H NMR data (see Experimental). Finally two tremetone derivatives have been isolated. The less polar one shows ^{1}H NMR signals very similar to those of 6-hydroxytremetone. However, a multiplet overlapping the signal of 11-H indicates that a hydroxyl group must be located at C-3. To determine the configuration, this compound was acetylated. The ^{1}H NMR spectrum of the resulting diacetate shows that the substituents at C-2 and C-3 are *cis* to each other. Therefore the ketone must have the structure **18**; while the absolute stereochemistry has not been proved, that shown is of toxol.

The second compound, molecular formula $C_{13}H_{16}O_3$, displays typical ^{1}H NMR signal of a 3,4-disubstituted acetophenone (see Experimental), indicating again that a tremetone derivative may be present. A doublet at 3.22 (2H, $J = 9$ Hz) collapses to a singlet on irradiation of the triplet at 4.72 ppm (1H) indicating the presence of a dihydrobenzofuran. The methyl singlets at 1.37 and 1.24 ppm show that the isopropylidene group is most probably hydrated and that the second compound must have the structure **19**. In agreement with this assumption, loss of acetone can be observed in the mass spectrum. The absolute configuration at C-2 again has not been determined. Racemic **19** has been synthesized [17].

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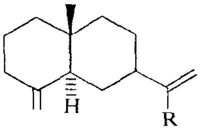
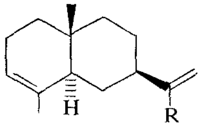
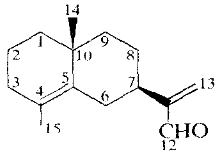
* Part 268 in the series "Naturally Occurring Terpene Derivatives". For Part 267 see Rustaiyan, A., Nazarians, L. and Bohlmann, F. (1980) *Phytochemistry* **19**, 1230.



1 R = Me **2** R = CO_2H[12] [16]
3 R = CHO[13]



4 R = Me[16]
5 R = CO_2H[14]



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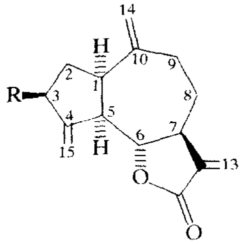
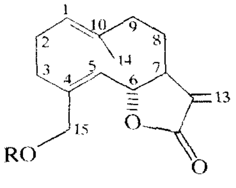
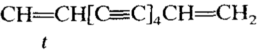


7 R = H[5]
8 R = OiVal[6]
9 R = OMebu

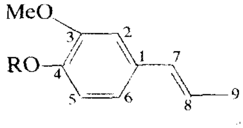


10 R = iBu **11** R = Mebu

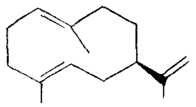


$RCH{=}CH[C{\equiv}C]_4CH{=}CH_2$
t

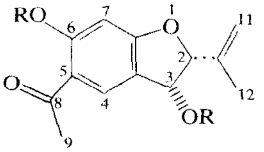
12 R = Me[8] **13** R = CHO[8]
14 R = CH_2OAc[8]



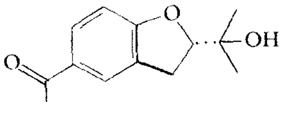
15 R = Mebu **16** R = iVal[9]



17 [15]



18 R = H **18a** R = Ac



19

A survey of the constituents of *F. speciosa* shows a close biogenetical relationship between the sesquiterpenes isolated from this species. Germacrene A (**17**), which is relatively rare in composites, is the common precursor of the eudesmane derivatives **1–6** and of the lactones **10** and **11**, while **7–9** are clearly formed by cyclization of the corresponding 10-membered ring lactones, themselves also formed from **17**. Though these combinations of biogenetic pathways can be found in many composites, the high concentrations of

Table 1. ^{1}H NMR data of **9–11** (270 MHz, $CDCl_3$, TMS as internal standard)

	9	**10**	**11**	
1-H	2.95, *ddd*		4.92,*m*	
3-H	5.59, *dd(br)*			
5-H	2.45, *m*		4.94, *d(br)*	
6-H	4.08, *dd*		4.59, *dd*	
7-H	2.87, *dd(br)*		2.55, *m*	
13-H	6.23, *d*		6.29, *d*	
13'-H	5.51, *d*		5.55, *d*	
14-H	4.98, *s(br)*		1.39, *s(br)*	
14'-H	4.96, *s(br)*			
15-H	5.47, *s(br)*	4.62, *s(br)*		4.60, *s(br)*
15'-H	5.28, *dd*			
OCOR	2.42, *tq*	2.58, *qq*		2.50, *tq*
	1.76, *dqq*	1.20, *d*		1.70, *m*
	1.48, *dqq*			1.45, *m*
	0.95, *t*			0.94, *t*
	1.18, *d*			1.18, *d*

J(Hz): **9**: 1,2 = 1.5 ~ 8; 2,3 = 2',3 = 7; 3,15 = 5,15 ~ 2; 5,6 = 6,7 = 9.5; 7,8 = 10; 7,13 = 3.5; 7,13 = 3.2; **10/11** 5,6 = 6,7 ~ 10; 7,13 = 3.5; 7,13 = 3.

2, **5** and **7** are unusual. Concerning relationships to other groups, the acetylenes **12**–**14** and the isoeugenol derivatives **15** and **16** may be more important. Such combinations of constituents are typical for several genera belonging to the subtribe Coreopsidinae [8, 9], though **16** itself so far has only been isolated from a *Felicia* species [10], tribe Astereae, where, however, compounds like **12**–**14** have never been isolated. Sesquiterpene lactones are rare in the subtribe Coreopsidinae. Only from two *Cosmos* species, costunolide has been isolated [11], while other subtribes of the Heliantheae show a large variety of sesquiterpene lactones. *p*-Hydroxyacetophenones, like **18** and **19**, have been isolated from many tribes, but not from species belonging to the Coreopsidinae. The overall picture therefore is in agreement with some relationship between *Fitchia* and the Coreopsidinae but it is not particularly close.

EXPERIMENTAL

IR: CCl_4; ^1H NMR: 270 MHz; MS: 70 eV. The air-dried plant material was extracted with Et_2O–petrol (1:2) and the resulting extracts were first separated by CC (Si gel, act. grade II) and further by repeated TLC (Si gel GF 254). Known compounds were identified by comparison of the IR and ^1H NMR spectra with those of authentic material. 300 g leaves afforded 7 g **7** and 60 mg of a mixture of **8**–**11** (Et_2O–petrol, 1:1) (relation 1:5:5:5). By TLC with $AgNO_3$-impregnated Si gel, **8** and **9** could be separated from **10** and **11**. While **8** and **9** could not be completely separated after repeated TLC, **10** and **11** could be largely separated. 900 g of the stems yielded 2 mg **1**, 2.5 g **2**, 5 mg **4**, 2.5 g **5** and 20 mg **7**. 220 g roots afforded 5 mg **3**, 5 mg **6** (Et_2O–petrol, 1:10), 100 mg **7**, 0.2 mg **12**, 0.2 mg **13**, 0.1 mg **14**, 5 mg **15** (Et_2O–petrol, 1:10), 5 mg **16**, 8 mg **17**, 6 mg **18** (Et_2O–petrol, 2:1) and 4 mg **19** (Et_2O–petrol, 2:1).

Zaluzanin-C-[2-*methylbutyrate*] (**9**). Colourless gum, not free from **6**. IR cm^{-1}: 1780 (γ-lactone), 1750 (CO_2R). MS: M^+ *m/e* 332.199 (1%) ($C_{20}H_{28}O_4$); $-C_4H_9CO_2H$ 230 (18); C_4H_9CO+ 85 (100).

15-*Isobutyryloxycostunolide* (**10**). Colourless gum, IR cm^{-1}: 1785 (γ-lactone), 1750 (CO_2R). MS: M^+ *m/e* 318.183 (1%) ($C_{19}H_6O_4$); $-C_3H_7CO_2H$ 230 (24); $C_3H_7CO^+$ 71 (100).

15-[2-*Methylbutyryloxy*]-*costunolide* (**11**). Colourless gum. IR cm^{-1}: 1785 (γ-lactone), 1750 (CO_2R). MS: M^+ *m/e* 332.199 (1%) ($C_{20}H_{28}O_4$): $-C_4H_9CO_2H$ 230 (28); $C_4H_9CO^+$ 85 (100).

Iso-β-*costal* (**6**). Colourless oil, not free from **3**, IR cm^{-1}: 2740, 1700 (CHO). MS: M^+ *m/e* 218.167 (100%) ($C_{15}H_{22}O$); $-{}^{\cdot}Me$ 203 (90); $-{}^{\cdot}CHO$ 189 (42). ^1H NMR: δ 2.57 (*m*, 7-H), 9.50 (*s*, 12-H), 6.24 and 5.93 (*s*(*br*), 13-H), 1.25 (*s*, 14-H), 1.53 (*s*(*br*), 15-H).

Isoeugenol-[2-*methylbutyrate*] (**15**). Colourless oil, not free from **16**, IR cm^{-1}: 1770 (PhOCOR), 1610, 1510 (aromatic), 1650, 970 (*trans* CH═CH). MS: M^+ *m/e* 248.141 (12%) $C_{15}H_{20}O_3$); $-O{=}C{=}C(Me)Et$ 164 (100). ^1H NMR: δ 6.93 (*s*(*br*), 3-H), 6.94 (*d*(*br*), 5-H, *J* = 8 Hz), 6.89 (*d*, 6-H, *J* = 8 Hz); 6.37 (*dq*, 7-H, *J* = 15, 1.5 Hz), 6.18 (*dq*, 8-H, *J* = 15, 6.5), 1.88 (*dd*, 9-H, *J* = 6.5, 1.5 Hz); 3.82 (*s*, OMe); 2.66 (*tq*, 2-H, *J* = 7.7 Hz), 1.6 and 1.4 (*m*, 3-H); 1.04 (*t*, 4-H, *J* = 7 Hz); 1.30 (*d*, 5-H).

6-*Hydroxytoxol* (**18**). Colourless oil, IR cm^{-1}: 3500–2600 (OH), 1645 (PhCO); UV Et_2O λ_{max} nm: 318, 276; MS: M^+ *m/e* 234.089 (100%) ($C_{13}H_{14}O_4$); $-H_2O$ 216 (62); 216 $-{}^{\cdot}Me$ 201 (80); ^1H NMR ($CDCl_3$): δ 12.99 (*s*, OH), 7.83 (*s*, 4-H), 6.46 (*s*, 7-H), 5.27 (*s*(*br*), 11-H), 5.21 (*s*(*br*), 11-H), 5.18(*m*, 2-H), 5.05 (*M*, 3-H), 2.59 (*s*, 9-H), 1.92 (*s*(*br*), 12-H); 6 mg **18** in 0.5 ml $CHCl_3$ were heated after addition of 5 mg 4-pyrrolidinopyridine for 30 min at 70°. Usual work-up afforded 5 mg **18a**, colourless oil, ^1H NMR ($CDCl_3$): δ 7.94 (*s*, 4-H), 6.66 (*s*, 7-H), 6.33 (*d*, 3-H, *J* = 6.5 Hz), 5.21 (*s*(*br*), 11-H), 5.15 (*s*(*br*), 11-H), 5.17 (*d*, 2-H, *J* = 6.5 Hz), 2.51 (*s*, 9-H), 1.82 (*s*(*br*), 12-H), 2.36 (*s*, PhOAc), 2.04 (*s*, OAc). $[\alpha]_D + 42.2°$ (*c* 0.5, $CHCl_3$).

10,11-*Dihydro*-10-*hydroxytremetone* (**19**). Colourless oil, IR cm^{-1}: 3600 (OH), 1680 (PhCO), 1606, 1590 (aromatic). UV (Et_2O) nm: 272, $[\alpha]_D$ −16.0° (*c* 0.3, $CHCl_3$). MS: M^+ *m/e* 220.110 (49%) ($C_{13}H_{16}O_3$); $-{}^{\cdot}Me$ 205 (8); $-H_2O$ 202 (6); $-Me_2CO$ 162 (100) $-H_2O$ 187 (25); 162 $-{}^{\cdot}Me$ 147(100); 147 − CO 119(85). ^1H NMR ($CDCl_3$): δ 4.72 (*t*, 2-H, *J* = 9 Hz), 3.22 (*d*, 3-H, *J* = 9 Hz); 7.83 (*s*(*br*), 4-*H*), 7.81 (*dd*, 6-H, *J* = 8, 1.5 Hz), 6.82 (*d*, 7-H, *J* = 8 Hz), 2.54 (*s*, 9-H), 1.37 (*s*, 11-H), 1.24 (*s*, 12-H).

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