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DITERPENES FROM *KOANOPHYLLON* SPECIES*

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Key Word Index—*Koanophyllon admantium*; *K. conglobatum*; Compositae; Eupatorieae; diterpenes; clerodanes; geranylgeraniol derivatives.

Abstract—The investigation of two *Koanophyllon* species afforded, in addition to known compounds, several new diterpenes, two new geranylgeraniol derivatives and four diterpenes, most probably closely related to clerodanes; their structures, however, could not be deduced with certainty. The chemotaxonomic situation of this genus is discussed briefly.

INTRODUCTION

The genus *Koanophyllon* (Compositae) is placed in the tribe Eupatorieae (subtribe Critoniinae) [1, 2]. So far nearly nothing is known about the chemistry of this genus, only α-humulene being isolated from *K. standleyi* [3]. We now have investigated two species from Brazil, *K. admantium* and *K. conglobatum*, which gave, in addition to widespread sesquiterpene hydrocarbons and triterpenes, several more characteristic diterpenes, which may be of chemotaxonomic value.

RESULTS AND DISCUSSION

While the roots of *K. admantium* (Gardn.) K. et R. only afforded dammaradienyl acetate, the aerial parts gave germacrene B and D, α-humulene, caryophyllene, squalene, lupeol and its acetate together with its Δ12,13-isomer, friedelin, β-amyrin acetate, the furano-diterpenic acids with unestablished absolute configuration, **1** [4], **2** [4] and **3** [5] as well as a further diterpene **8a**, which only could be isolated as its methyl ester **8b**. The structure of **8b** could be deduced from the ^{1}H NMR data (Table 1). The position of the acetoxy group directly followed from the corresponding ^{1}H NMR doublet at δ 4.59, while the configuration of the 2,3-double bond was deduced from the observed chemical shifts of H-2 and H-20, if compared with those of known geranylgeraniol derivatives. The position of the carbomethoxy group also followed from the ^{1}H NMR data. All olefinic methyls showed an allylic coupling with different olefinic protons, as shown by spin decoupling. Therefore the ester group has to be placed at C-15. The configuration of the 14,15-double bond could be deduced from the chemical shift of H-14. The assignment of the configurations of the two remaining double bonds was also deduced by comparing the corresponding chemical shifts with those of geranylgeraniol and similar compounds. We have named **8a** koanoadmantic acid.

Table 1. ^{1}H NMR spectral data of compounds **8b** and **9** ($CDCl_3$, 270 MHz, TMS as internal standard)

	8b	**9**
H-1	4.59 *d* (*br*)	3.69*
H-2	5.35 *t* (*br*)	1.4 *m*
H-4	2.05 *m*	
H-5		
H-6	5.13 *t* (*br*)	5.12 *t* (*br*)
H-8	2.05 *m*	2.02 *m*
H-9		
H-10	5.10 *t* (*br*)	5.25 *t* (*br*)
H-12	2.05 *m*	3.03 *s* (*br*)
H-13	2.56 *dt* (*br*)	—
H-14	5.93 *t* (*br*)	6.12 *s* (*br*)
H-16	1.89 *s* (*br*)	1.88 *d*
H-17	—	2.14 *d*
H-18	1.60 *s* (*br*)	1.61 *s* (*br*)
H-19		1.60 *s* (*br*)
H-20	1.71 *s* (*br*)	0.92 *d*
OAc	2.05 *s*	—
OMe	3.75 *s*	—

* Two overlapped double triplets.
J(Hz): 1,2 = 5,6 = 9,10 = 13,14 = 7; compound **9**: 3,20 = 6.

The aerial parts of *K. conglobatum* (DC.) K. et R. afforded germacrene D, sitosterol and again several diterpenes. The structure of a further geranylgeraniol derivative (**9**) clearly followed from the ^{1}H NMR data (Table 1). The downfield shifted methyl signals for H-16 and H-17, that of H-14 and the presence of a broadened singlet at 3.03 ppm required a conjugated keto group at C-13, while a complex signal at 3.69 ppm and a doublet at 0.92 ppm were only in agreement with a 2,3-dihydro derivative of 13-oxo-geranylgeraniol. The configuration at C-3 was not determined. The main constituent was a very labile furano-diterpenic acid. The presence of a β-substituted furan clearly followed from the ^{1}H NMR data

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* Part 354 in the series "Naturally Occurring Terpene Derivatives". For Part 353 see Bohlmann, F., Jakupovic, J., Müller, L. and Schuster, A. (1981) *Angew. Chem.* (in press).

(Table 2), while the substitution pattern of the decalin part caused difficulties. The ^{13}C NMR data of the acid and the Eu(fod)$_3$-induced shifts in the spectrum of the methyl ester agreed best with the structure **4a** for the natural compound. In particular, the shifts of the signals of the olefinic proton and of the broadened doublet at 2.32 ppm required a position of these hydrogens near the ester group. Also the shifts of the methyl signals agreed with this proposal. In a clerodane with a 1,10-double bond the shift of the olefinic proton signal should be smaller. Biogenetic consideration also supported this assumption. As the clerodanes, which were present in the first *Koanophyllon* species, are formed most probably from labdanes via rearrangements (see Scheme 1) [4], **4a** would be the result of proton elimination of the intermediate **11**, while migration of the C-4 methyl would lead to **12**, which would give **3** after proton elimination.

The ^1H NMR data of **5b**, obtained by acetylation of the natural compound, and those of the inseparable esters **6b** and **7b**, obtained by esterification of the natural acids (Table 2), show that these compounds have the same carbon skeleton as **4a**. The molecular formula of **5c** is $C_{21}H_{36}O_3$, indicating the presence of a hydroxyl group, its presence also following from the IR band (3620 cm^{-1}) and from the broadened triplet at 3.66 ppm in the ^1H NMR spectrum of **5c**, which was shifted to 4.10 ppm in the spectrum of the corresponding acetate **5b** (Table 2). An additional doublet for a secondary methyl (0.93 ppm) was obviously that of H-16. Therefore the side chain in **5a** most probably was $-CH_2CH_2CH(Me)CH_2CH_2OH$, only the stereochemistry at C-13 not being determined. In the mass spectrum of **5c** loss of this moiety leading to the base peak at *m/z* 235 was in agreement with this. The IR spectrum of the mixture of **6b** and **7b** clearly showed the presence of γ-lactones, while the molecular formula was $C_{21}H_{30}O_4$ for both methyl esters. Therefore **6b** and **7b** were isomers. From the ^1H NMR data (Table 2) it was deduced that **6b** was a lactone with a β-olefinic proton (H-14, 7.11, *t*, $J = 1.5$ Hz), while **7b** was a lactone with an α-olefinic proton (H-16, 4.76, *d*, $J = 1.5$ Hz). The observed couplings and the chemical shifts showed that only the proposed side chain agreed with these findings, especially when compared with data of similar compounds [6]. Again loss of the proposed side chain led to *m/z* 235 in the mass spectrum of **6b**/**7b** followed by loss of ·CO_2Me leading to *m/z* 175. The absolute configuration of all diterpenes was not determined. We have named **4a**–**7a** koanophyllic acid A, B, C and D respectively.

Table 2. ^1H NMR spectral data of compounds **4b**, **5b**, **6b** and **7b**

	4b	Δ	**5b**	**6b**	**7b**
H-1					
H-2					
H-3					
H-6	5.61 *d* (*br*)	0.30	5.67 *d* (*br*)	5.61 *d* (*br*)	
H-10	2.32 *d* (*br*)	0.94	2.23 *d* (*br*)	2.22 *d* (*br*)	
H-12	2.34 *t* (*br*)	0.15		2.33 *t* (*br*)	
H-13	—	—		—	
H-14	6.27 *s* (*br*)	0.05		7.11 *t*	5.85 *t*
H-15	7.34 *dd*	0.03	4.10 *t* (*br*)	4.78 *d*	—
H-16	7.21 *s* (*br*)	0.06	0.93 *d*	—	4.76 *d*
H-17	0.89 *d*	0.11	0.84 *d*	0.88 *d*	
H-19	1.31 *s*	0.57	1.38 *s*	1.33 *s*	
H-20	0.70 *s*	0.15	0.67 *s*	0.73 *s*	0.75 *s*
OMe	3.64 *s*	0.75	—	3.65 *s*	
OAc	—	—	2.06 *s*	—	—

J(Hz): Compound **4b**: 1β,10 = 12.5; 6,7 = 4; 8,17 = 6.5; 11,12 = 8 and 9; 14,15 = 15,16 = 1.5; compound **5b**: 1β,10 = 12; 6,7 = 4; 8,17 = 7; 13,16 = 6; 14,15 = 6; compounds **6b**/**7b**: 1β,10 = 12; 6,7 ~ 4; 8,17 = 7; 11,12 = 8 and 9; 14,15 = 1.5; (**7b**: 14,16 = 1.5).

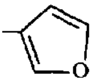
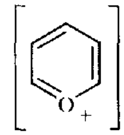
The compounds isolated from the two *Koanophyllon* species show that acyclic and dicyclic diterpenes may be characteristic for this genus. So far, labdane derivatives have been isolated from *Critonia* [3] and an *Aristeguietia* species [7]. More common compounds such as euparin-like ketones, were present in *Critonia* [3], *Ophryosporus* [7], *Fleischmanniopsis* [3] and *Cronquistianthus* species [8, 9], while so far only from one *Critonia* species [5] have sesquiterpene lactones been reported. However, many genera of this subtribe have not yet been investigated at all. Further studies are necessary to obtain a clearer picture of the chemotaxonomy of the whole subtribe.

EXPERIMENTAL

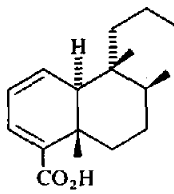
The air-dried plant material was extracted with Et_2O–petrol (1:2) and the resulting extracts were separated by column chromatography (Si gel) and further by repeated TLC (Si gel). Known compounds were identified by comparing the IR and ^1H NMR spectra with those of authentic material.

Koanophyllon admantium (*voucher RMK* 8162). The roots (37 g) afforded 8 mg dammaradienyl acetate and the aerial parts (175 g) 2 mg germacrene D, 8 mg germacrene B, 2 mg α-humulene, 2 mg caryophyllene, 12 mg squalene, 20 mg lupeol, 80 mg of its acetate, 80 mg of its Δ12,13 isomer, 40 mg β-amyrin acetate, 40 mg friedelin, 20 mg **1**, 50 mg **2**, 20 mg **3** and 10 mg **8a**, purified as its methyl ester **8b** (CH_2N_2, TLC: Et_2O–petrol, 1:1).

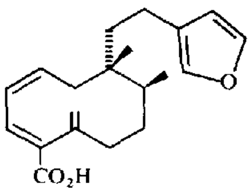
Koanophyllon conglobatum (*voucher RMK* 8030). The aerial parts (200 g) afforded 50 mg germacrene D, 3 mg sitosterol, 1 g **4a**, 18 mg **5a**, 1 mg **6a**, 5 mg **7a** and 5 mg **9**. **4a**, **6a** and **7a** were transformed to their methyl esters by addition of diazomethane and purified by TLC (Et_2O–petrol, 1:1), while **5a** was acetylated and purified as its acetate (TLC: Et_2O–petrol, 3:1).

Koanophyllic acid A (**4a**). Colourless gum, which rapidly polymerized, MS *m/z* (rel. int.): 316.204 $[M]^+$ (0.3), 221 [M − ·CH_2CH_2–  (A)]$^+$ (77), 175 $[221 - HCO_2H]^+$ (48), 81  (100); ^{13}C NMR ($CDCl_3$) (C-1 through C-20): 18.4 *t*, 27.3 *t*, 37.8 *t*, 48.7 *s*, 138.8 *s*, 121.1 *d*, 29.7 *t*, 33.4 *d*, 37.4 *s*, 42.2 *d*, 31.5 *t*, 23.5 *t*, 125.8 *s*, 11.0 *d*, 138.5 *d*, 141.6 *d*, 16.6 *q*, 187.4 *s*, 25.2 *q*, 15.3 *q* (some signals may be interchangeable); $[\alpha]_D$ −16° ($c = 0.9$, $CHCl_3$). Addition of CH_2N_2 afforded **4b**, colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1725 (CO_2R), 1500, 880 (furan); MS *m/z* (rel. int.): 330 $[M]^+$ (3), 235 $[M - A]^+$ (100), 175 $[235 - HCO_2Me]^+$ (66).

Koanophyllic acid B (**5a**). Colourless gum which was transformed to the methyl ester **5c** and the acetate **5b**. **5c**: Colourless gum; MS *m/z* (rel. int.): 336.266 $[M]^+$ (4) ($C_{21}H_{36}O_3$), 321 $[M - Me]^+$ (0.5), 277 $[M - CO_2Me]^+$ (6), 235 $[M - CH_2CH_2CH(Me)CHCHOH]^+$ (100), 175 $[235 - HCO_2Me]^+$ (58); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1735 (CO_2R);



1



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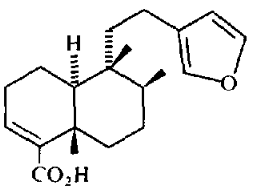

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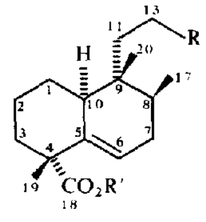
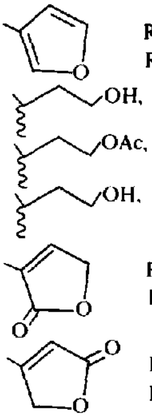
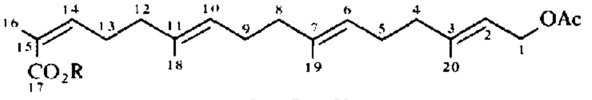
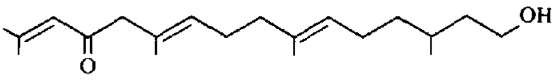




4a R = R' = H
4b R' = Me
5a R = R' = H
5b R = R' = H
5c R = R' = Me
6a R = R' = H
6b R' = Me
7a R = R' = H
7b R' = Me



8a R = H
8b R = Me



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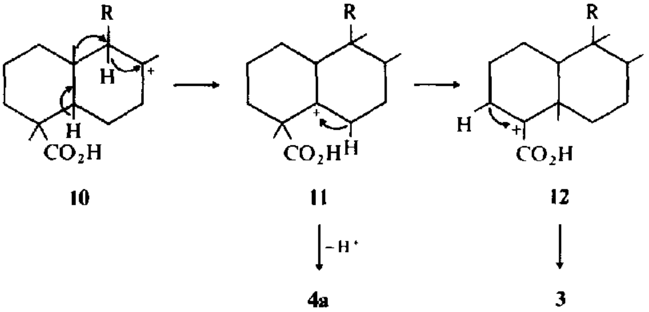

Scheme 1.

5b: Colourless gum, MS *m/z* (rel. int.): 318 $[M - HCO_2H]^+$ (9), 221 $[M - {}^{\cdot}CH_2CH_2CH(Me)CH_2CH_2OAc]^+$ (79), 177 $[221 - CO_2]^+$ (100); CI (*iso*-butane): 365 $[M+1]^+$ (28), 319 $[365 - HCO_2H]^+$ (100); $[\alpha]_D$ −18.2 (c = 0.65, $CHCl_3$).

Koanophyllic acids C and D (**6a** *and* **7a**). Inseparable, colourless gum, which was esterified with CH_2N_2 affording a mixture of **6b** and **7b**, which could not be separated, colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1785, 1755 (γ-lactone), 1730 (CO_2R); MS *m/z* (rel. int.): 346.214 $[M]^+$ (6) ($C_{21}H_{30}O_4$), 287 $[M - CO_2Me]^+$ (12), 235 $[M^+ - {}^{\cdot}CH_2CH_2C_4H_3O_2]^+$ (80), 204 $[235 - OMe]^+$ (5), 189 $[204 - Me]^+$ (4), 175 $[235 - HCO_2Me]^+$ (100).

Koanodmantic acid methyl ester (**8b**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1235 (OAc), 1720 (C=CCO_2R); MS *m/z* (rel. int.): 316.240 $[M - HOAc]^+$ (5) ($C_{21}H_{32}O_2$), 301 $[326 - Me]^+$ (2), 181 $[M - CH_2C(Me){=}CH(CH_2)_2C(Me){=}CHCH_2OAc]^+$ (4), 149 $[181 - MeOH]^+$ (30), 121 $[149 - CO]^+$ (100).

13-Oxo-2,3-dihydro-geranylgeraniol (**9**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1720 (C=CCO); MS *m/z* (rel. int.): 306.256 $[M]^+$ (2) ($C_{20}H_{34}O_3$), 291 $[M - Me]^+$ (1), 83 $[C_4H_7CO]^+$ (100); $[\alpha]_D$ −1.6 (c = 0.5, $CHCl_3$).

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REFERENCES

1. Robinson, H. and King, R. M. (1977) *The Biology and Chemistry of the Compositae* (Heywood, V. H., Harborne, J. B. and Turner, B. L., eds.) p. 458. Academic Press, London.
2. King, R. M. and Robinson, H. (1980) *Phytologia* **46**, 446.
3. Bohlmann, F., Zitzkowski, P., Suwita, A. and Fiedler, L. (1978) *Phytochemistry* **17**, 2101.
4. Bohlmann, F. and Fritz, U. (1978) *Phytochemistry* **17**, 1769.
5. Misra, R., Pandey, R. C. and Dev, S. (1968) *Tetrahedron Letters* 2681.

6. Bohlmann, F., Zdero, C., Gupta, R. K., King, R. M. and Robinson, H. (1980) *Phytochemistry* **19**, 2695.
7. Bohlmann, F. and Zdero, C. (1978) *Phytochemistry* **18**, 145.
8. Christensen, W. C. (1965) *Econ. Botany* **19**, 293.
9. Zalkow, L. H., Gelbaum, L., Ghosai, M. and Fleischmann, T. J. (1977) *Phytochemistry* **16**, 1313.
10. Bohlmann, F., Jakupovic, J. and Lonitz, M. (1977) *Chem. Ber.* **110**, 301.