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# FURANOEREMOPHILANES FROM *GYNOXYS* SPECIES

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IN HONOUR OF PROFESSOR ANTONIO G. GONZALEZ

**Key Word Index**—*Gynoxys acostae*; *G. buxifolia*; *G. nitida*; Compositae; furanoeremophilanes; sesquiterpenes.

**Abstract**—Five new furanoeremophilanes were isolated from three *Gynoxys* species. The structures of three 3α,6β-diacyloxyfuranoeremophilanes previously isolated from *G. sancto-antonii* have to be revised to the corresponding 1β,6β derivatives.

## INTRODUCTION

The position of the genus *Gynoxys* in the tribe Senecioneae is questionable. In the modified version [1] of the system of Jeffrey *et al.* [2] it has been placed in the woody cacaloid group. Chemical investigation of the members of this group gave mainly furanoeremophilanes. Previous results from *Gynoxys* species showed 10β-H furanoeremophilanes with functional groups at C-3 and C-6 to be the most common constituents [3–5]. Surprisingly *G. oleifolia* produces diterpenes of the kaurane type [6]. While furanoeremophilanes are widespread within the whole tribe and 10β-H-3β,6β-dioxyfuranoeremophilanes are found in genera belonging to different groups, the diterpenes are rare. In this report we present our results from three further species.

## RESULTS AND DISCUSSION

The aerial parts of *Gynoxys acostae* Cuatr. provided the furanoeremophilanes **2**–**7**. While compounds **2**–**5** were obtained pure, all attempts to separate **6** and **7** failed. The spectral data of **2** and **3** were identical to those of **9** and **10** compounds previously isolated, along with **8**, from *G. sancto-antonii* [5]. The $^1$H NMR data of all compounds differed from each other mainly in the signals of the ester residues (Table 1). In the spectrum of **2** an acetate and an angelate, easily recognized by their typical signals, were present. An ester residue has to be placed at C-6, as indicated by the characteristic singlet for an isolated oxymethyne group. The couplings of the other downfield signal at δ4.71 *ddd*($J$ = 5, 10, 10 Hz) required an axial position. In structural formulae with a 3α-acyloxy substituent, and by assuming the usual chair conformation, H-10 should be axial with regard to ring B in both the 10α and 10β series. Because both compounds exhibited a $J_{9,10}$ couplings indicative of the presence of a 10β-H furanoeremophilane with an equatorial H-10 in ring B, we checked the structures again by careful examination of all spectral data and by spin decoupling. At ambient temperature all signals in the $^1$H NMR spectra were broadened. By heating the sample slightly above ambient temperature all signals sharpened. Decoupling experiments starting with the well-separated H-9 signals allowed the assignment of H-10. Upon irradiation the latter influenced the signal at δ4.71, which thus corresponds to H-1. The relative positions of the ester residues were deduced from the results of NOE difference experiments and confirmed by an HMBC experiment. In particular the NOE effect between H-13 and acetate methyl (4%) required a 6-acetoxy group. Further NOEs were observed between H-6 H-1 (8%), H-13 (1.5%) and H-3α (7%) as well as between H-14/15 H-9β (4%) and H-10 (10%). The energy-minimized conformation, calculated using a molecular modelling program [7], is in excellent agreement with spectroscopic facts. The relative positions of the ester residues in **3**, **6** and **7** were deduced from the diagnostic chemical shifts for H-1 and H-6, depending on the ester group. From the spectra of **2**, **4** and **5**, the following conclusions could be drawn. H-6 resonates at δ6.47 in a 6-angelate, and at δ6.37 in a 6-senecioate, while at 1-angelate shifts H-1 to δ4.70 and a 1-senecioate to δ4.63. H-6 in 6-acetate is at highest field. Likewise, the signals for the ester residues differed markedly, depending on position, being shifted downfield at C-6 position. The assignment of signals for the mixture of **6** and **7** was possible as they were present in different concentrations. In Table 1 the corrected data of **1** (**8** in ref. 5) are added.

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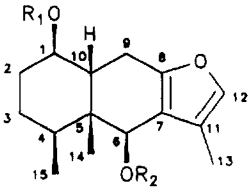
Table 1. $^1$H NMR data of **1**–**7** and **11** ($CDCl_3$, 400 MHz, internal standard residual $CHCl_3$ solvent peak = 7.26 ppm)

| Proton | **1*** | **2** | **3** | **4** | **5** | **6** | **7** | mult† | **11**‡ |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 4.65 | 4.71 | 4.61 | 4.71 | 4.63 | 4.70 | 4.64 | *ddd* | 1.65 *m*, 1.49 *m* |
| 2α | | 2.01 | 1.97 | 2.03 | 2.00 | 2.00 | 2.00 | *dddd* | 1.90 *m* |
| 2β | | 1.57 | 1.52 | 1.56 | 1.52 | 1.55 | 1.55 | *dddd* | 1.65 *m* |
| 3α | | 2.16 | 2.15 | 2.24 | 2.17 | 2.20 | 2.20 | *brdddd* | 5.35 *ddd* |
| 3β | | 1.47 | 1.43 | 1.47 | 1.46 | 1.47 | 1.47 | *dddd* | — |
| 4 | | 1.64 | 1.62 | 1.67 | 1.67 | 1.66 | 1.66 | *m* | 1.90 *m* |
| 6 | 6.35 | 6.34 | 6.35 | 6.46 | 6.37 | 6.38 | 6.47 | *br s* | 6.42 *br s* |
| 9α | | 2.58 | 2.57 | 2.60 | 2.57 | 2.59 | 2.59 | *br dd* | 2.33 *br dd* |
| 9β | | 1.68 | 2.65 | 2.69 | 2.65 | 2.68 | 2.67 | *br ddd* | 2.85 *br dd* |
| 10 | | 2.22 | 2.17 | 2.24 | 2.17 | 2.22 | 2.20 | *ddd* | 2.11 *m* |
| 12 | 7.03 | 7.03 | 7.03 | 7.03 | 7.03 | 7.02 | 7.02 | *br s* | 7.03 *br s* |
| 13 | 1.85 | 1.87 | 1.85 | 1.82 | 1.81 | 1.82 | 1.81 | *d* | 1.82 *d* |
| 14 | 1.02 | 1.02 | 1.00 | 1.05 | 1.01 | 1.02 | 1.04 | *s* | 1.05 *s* |
| 15 | 1.02 | 1.02 | 1.01 | 1.03 | 1.00 | 1.01 | 1.02 | *d* | 0.96 *d* |
| $OR_1$ | 6.84 | 6.02 | 5.64 | 6.03 | 5.64 | 6.03 | 5.64 | *qq* | 6.88 *qq* |
| | 1.78 | 1.95 | 2.12 | 1.96 | 2.13 | 1.96 | 2.14 | *dq* | 1.79 *dq* |
| | 1.81 | 1.88 | 1.88 | 1.88 | 1.88 | 1.87 | 1.88 | *dq* | 1.87 *br s* |
| $OR_2$ | 2.11 | 2.11 | 2.11 | 6.12 | 5.72 | 5.73 | 6.12 | *s*(*qq*) | 5.65 *qq* |
| | | | | 2.01 | 2.20 | 2.20 | 2.02 | *d*(*dq*) | 2.16 *d* |
| | | | | 1.91 | 1.91 | 1.91 | 1.91 | *d*(*dq*) | 1.87 *br s* |

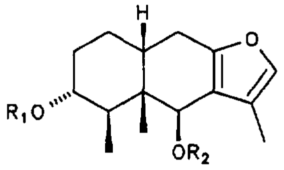
*Data taken from [5].

†Multiplicity from the spectrum of 2 at 40°; same multiplicity for **1**–**7**.

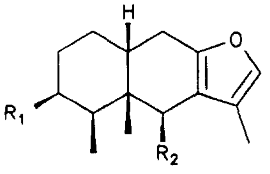
‡at 60°.



| | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| $R_1$ | Tigl | Ang | Sen | Ang | Sen | Ang | Sen |
| $R_2$ | Ac | Ac | Ac | Ang | Sen | Sen | Ang |



| | 8 | 9 | 10 |
|---|---|---|---|
| $R_1$ | Tigl | Ang | Sen |
| $R_2$ | Ac | Ac | Ac |



| | 11 | 12 | 13 | 14 | 15 |
|---|---|---|---|---|---|
| $R_1$ | OSen | OAng | OAng | OSen | H |
| $R_2$ | OTigl | OH | H | H | OSen |

*Gynoxys buxifolia* (HBK) Cass gave, in addition to germacrene D and *p*-hydroxy-acetophenone, the new furanoeremophilane **11**. Broadening of all signals in the $^1$H NMR spectrum indicated again the presence of a *cis* eremophilane. Upon heating to 60° all signals sharpened and spin decoupling showed that a 3, 6 diester was present. A strong NOE effect between H-6 and H-3 confirmed the presence of a *cis* decalin with both ester groups in the *β*-position. Similar compounds have been obtained from other *Gynoxys* species [3, 4, 5]. The long-range correlations observed in HMBC experiment between protons at ester bearing carbons and corresponding carbonyls ensured their relative positions. Table 2 lists the $^{13}$C-NMR data of compounds **2**, **3** and **11**.

*Gynoxys nitida* Muschler gave in addition to some widespread compounds the eremophilanes **2**, **3** and **12**–**15**.

The present results revealed the chemotaxonomic importance of 10*β*-H eremophilanes for the genus *Gynoxys*. To date 3*β*,6*β*-functionalized 10*β*-H eremophilanes have

Table 2. $^{13}$C NMR data of **2**, **3** and **11** ($CDCl_3$, 100 MHz, internal standard $CDCl_3$ = 77.0 ppm)

| Carbon | **2** | **3** | **11** | Mult |
|---|---|---|---|---|
| 1 | 71.6 *d* | 70.8 *d* | 25.7 *t* | |
| 2 | 26.2 | 26.2 | 25.9 | *t* |
| 3 | 26.6 *t* | 26.6 *t* | 71.1 *d* | |
| 4 | 31.9 | 31.9 | 36.1 | *d* |
| 5 | 41.9 | 41.9 | 41.9 | *s* |
| 6 | 69.3 | 69.4 | 68.7 | *d* |
| 7 | 115.6 | 115.6 | 115.5 | *s* |
| 8 | 149.9 | 150.0 | 150.5 | *s* |
| 9 | 21.0 | 20.8 | 25.8 | *t* |
| 10 | 41.9 | 41.9 | 36.6 | *d* |
| 11 | 119.4 | 119.5 | 119.9 | *s* |
| 12 | 138.6 | 138.6 | 138.2 | *d* |
| 13 | 8.5 | 8.5 | 8.7 | *q* |
| 14 | 19.7 | 19.7 | 19.8 | *q* |
| 15 | 14.5 | 14.4 | 8.5 | *q* |
| $OR_1$ 1 | 167.3 | 166.0 | 165.7 | *s* |
| 2 | 128.0 *s* | 116.1 *d* | 116.6 *d* | |
| 3 | 137.7 *d* | 157.0 *s* | 155.8 *s* | |
| 4 | 15.7 | 27.4 | 27.3 | *q* |
| 5 | 20.6 | 20.2 | 20.2 | *q* |
| $OR_2$ 1 | 171.1 | 171.2 | 167.6 | *s* |
| 2 | 21.0 *q* | 21.0 *q* | 128.6 *s* | |
| 3 | | | 137.2 | *d* |
| 4 | | | 14.4 | *q* |
| 5 | | | 12.2 | *q* |

assigned with aid of 2D hetero correlated experiment.

been obtained from the genera *Senecio*, *Othonna*, *Lopholaena*, *Petasites*, *Paracalia* and *Farfugium*, whereas 1*β*,6*β* derivatives have been obtained only from *Gynoxys* species. Thus, the relative position of ester groups may be of taxonomic importance at the subtribal level. The isolation of kauranes is still unexplained and requires confirmation.

## EXPERIMENTAL

The air-dried plant material was extracted with $MeOH-Et_2O$–petrol 1:1:1 at room temp. After defatting (MeOH, − 20°) the extract was sepd by CC (silica gel) using a petrol/EtOAc gradient and further by HPLC and/or TLC. Known compounds were identified by comparision of the $^1$H NMR with those of authentic material.

Gynoxys *acostae*. Aerial parts, 530 g, collected in Ecuador, voucher RMK 10056, deposited in the U.S. National Herbarium. The CC fr. 1 (petrol–EtOAc, 19:1) contained 15 mg germacrene D and 3 mg bicyclogermacrene. Frs 2 (petrol–EtOAc, 9:1 and 4:1) and 3 (petrol–EtOAc, 1:1 and 1:4) were combined and sepd by TLC (petrol–EtOAc, 9:1) to give three broad bands. Band 1 ($R_f$ 0.6–0.8) was sepd by HPLC (RP 8, 250 × 8 mm, $MeOH-H_2O$, 5:1) and TLC (petrol–EtOAc, 97:3; 5 ×) to give 2 mg **4** and 5 mg of a mixture of **6** and **7**. Band 2 ($R_f$ 0.4–0.6), was purified by HPLC (the same conditions as above) to give 5 mg **5** ($R_t$ 5.1 min.). Band 3 ($R_f$ 0.1–0.3) was sepd by HPLC (as above) to give 10 mg spathulenol, a mixture ($R_t$ 3.1 min.) which by TLC (petrol–EtOAc, 19:1, 3 ×) gave 150 mg **2** and 100 mg **3** and 5 mg **5**.

Gynoxys buxifolia. Aerial parts, 370 g, collected in Ecuador, voucher RMK 10066, deposited in the U.S. National Herbarium. Analogous procedure as above yielded traces of germacrene D, 10 mg *p*-hydroxyacetophenone and 20 mg **11** (TLC, (petrol–EtOAc, 9:1 $R_f$ 0.45).

Gynoxys nitida. Aerial parts, 800 g, voucher RMK 9067, deposited in the U.S. National Herbarium. Analogous procedure gave 100 mg germacrene D, 20 mg bicyclogermacrene, 5 mg spathulenol, 420 mg oleanolic acid, 20 mg **2**, 20 mg **3**, 1200 mg **12**, 5 mg **13**, 2 mg **14** and 5 mg **15**.

1β,6β-*Diangeloyloxy*-10β*H-furanoeremophilane* (**4**). $\nu_{max}^{CCl_4}$: 1721, 1650 ($C{=}CCO_2R$), 1447, 1220, 1140; EIMS (probe)70 eV, *m/z* (rel. int.): 414.241 $[M]^+$ (3) (calc. for $C_{25}H_{34}O_5$: 414.241), 314 $[M - C_4H_7CO_2H]^+$ (3), 214 $[314 - C_4H_7CO_2H]^+$ (80), 172 (60), 83 $[C_4H_7CO]^+$ (100).

1β,6β-*Disenecioyloxy*-10β*H-furanoeremophilane* (**5**). $\nu_{max}^{CCl_4}$: 1720, 1650 ($C{=}CCO_2R$), 1447, 1225, 1141; EIMS (probe) 70 eV, *m/z* (rel. int.): 414.241 $[M]^+$ (2) (calc. for $C_{25}H_{34}O_5$: 414.241), 314 $[M - C_4H_7CO_2H]^+$ (3), 214 $[314 - C_4H_7CO_2H]^+$ (45), 172 (24), 83 $[C_4H_7CO]^+$ (100).

*Mixture of* 1β-*Angeloyloxy*-6β-*senecioyloxy- and* 1β-*senecioyloxy*-6β-*angeloyloxy*-10β*H-furanoeremophilane* (**6** and **7**). $\nu_{max}^{CCl_4}$: 1725, 1650 ($C{=}CCO_2R$), 1445, 1220, 1140; EIMS (probe) 70 eV, *m/z* (rel. int.): 414.241 $[M]^+$ (2) (calc. for $C_{25}H_{34}O_5$: 414.241), 314 $[M - C_4H_7CO_2H]^+$ (3), 214 $[314 - C_4H_7CO_2H]^+$ (55), 172 (35), 83 $[C_4H_7CO]^+$ (100).

3β-*Senecioyloxy*-6β-*tigloyloxy*-10β*H-furanoeremophilane* (**11**). $\nu_{max}^{CCl_4}$: 1717, 1653 ($C{=}CCO_2R$), 1450, 1388, 1263, 1146; EIMS (probe) 70 eV, *m/z* (rel. int.): 414.241 $[M]^+$(13) (calc. for $C_{25}H_{34}O_5$: 414.241), 314 $[M - C_4H_7CO_2H]^+$ (52), 231 $[314 - C_4H_7CO]$ (37), 214$[314 - C_4H_7CO_2H]^+$ (10), 83 $[C_4H_7CO]^+$ (100).

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