

8 β -TIGLOYLGUAIAGRAZIELOLIDE FROM CAMPOVASSOURIA BUPLEURIFOLIA

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Abstract—The polar parts of *Campovassouria bupleurifolia* afforded in addition to several known sesquiterpene lactones a further β -lactone and a germacranolide acid.

From the new South American monotypic genus *Campovassouria* (tribe Eupatorieae, subtribe Disynaphiinae [1]) so far kaurene derivatives have been isolated [2]. We now have reinvestigated the polar fractions of *C. bupleurifolia* (DC.) K. et R. to see whether relationships are visible to *Disynaphia* and *Grazielia* (= *Dimorpholepis*) placed in the same subtribe where special lactones were isolated [3–5].

Careful separation of the polar parts of the extract of the aerial parts by TLC and HPLC afforded the heliangolides **1** [4], **2** [6] and **3** [6], the germacrolides **4** [4] and **5** [7], the guaianolide **7** [8] and a further β -lactone, the 8 β -tigloyloxyguaiagrazielolide **8** as well as the acid **6**.

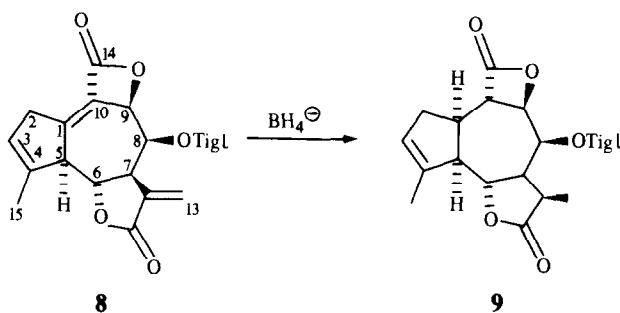
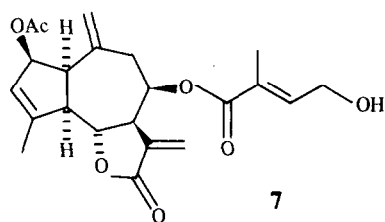
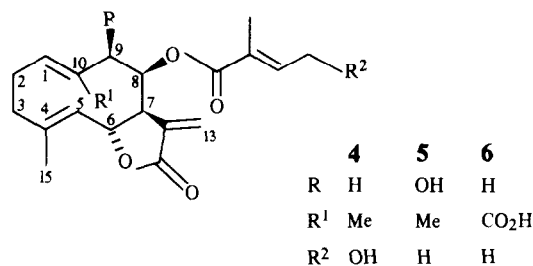
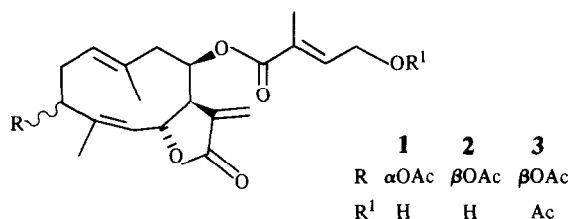
The structure of **8** followed from the molecular formula and the ^1H NMR spectral data (Table 1). The presence of a β -lactone could be deduced from the IR band at 1833 cm^{-1} while a γ -methylene lactone was indicated by the IR band and the typical ^1H NMR signals. The nature of the remaining oxygen function also followed from the typical ^1H NMR signals of a tiglate. Spin decoupling showed that the fourfold doublet at δ 3.15 was due to H-7 as the methylene doublets collapsed to singlets on irradiation of this signal. Furthermore the signals at δ 4.27 and 6.14 were altered indicating that these signals corresponded to H-6 and H-8. A pair of broadened doublets at δ 3.56 and 3.36 with a very large geminal coupling ($J = 24\text{ Hz}$) obviously were due to a methylene group between two double bonds. Spin decoupling showed that the corresponding protons were coupled with an olefinic signal at δ 5.65, with an olefinic methyl signal and with two further protons. These protons were due to H-5 and H-9 as followed from irradiation of H-6 and H-8 respectively. Thus the whole sequence was established leading to structure **8**. Sodium boranate reduction afforded the tetrahydro derivative **9** as followed from the molecular formula and the ^1H NMR spectral data (Table 1). The stereochemistry at C-11 was deduced from the coupling $J_{11,13}$ and that at C-10 from the couplings $J_{1,10}$ and $J_{9,10}$. The last two couplings only agreed with *trans*-couplings if models were inspected. This stereochemistry required an α -attack at C-1 by the boranate ion which also agreed with a model of **8** as the β -face was hindered by the quasi-axial

ester group at C-8 and protonation at 10β seemed to be thermodynamically favoured. Thus **8** was closely related to the corresponding β -lactone from *Grazielia intermedia* [3].

Table 1. ^1H NMR spectral data of compounds **6**, **8** and **9** (400 MHz, CDCl_3 , TMS as int. standard)

	8	9	6
H-1	—	2.83 dddd	5.84 br dd
H-2	3.56 br d	2.55 m	3.45 br dd
H-2'	3.36 br d		2.35 m
H-3	5.65 ddd	5.55 ddd	—
H-5	3.70 br d	2.64 m	4.97 br d
H-6	4.27 t	4.53 t	5.10 dd
H-7	3.15 dddd	2.11 m	2.89 br ddd
H-8	6.14 br d	5.72 dd	5.79 br d
H-9	5.04 ddt	4.74 dd	3.53 br dd
			2.22 br d
H-10	—	4.10 dd	—
H-11	—	2.64 dq	—
H-13	6.33 d	1.29 d	6.29 d
H-13'	5.77 d		5.64 d
H-15	2.00 ddt	1.91 br s	1.82 br s
OCOR	6.75 qq	6.90 qq	6.77 br q
	1.76 dq	1.84 dq	1.76 br d
	1.74 dq	1.88 dq	1.75 br s

J (Hz): Compound **6**: 1, 2 = 12; 1, 2' = 4; 2, 3 = 10; 2, 2' = 13; 2, 3' = 4; 5, 6 = 6, 7 = 10; 7, 8 ~ 1; 7, 13 = 3.5; 7, 13' = 3; 8, 9 = 6.5; 8, 9' = 14; compound **8**: 2, 2' = 24; 2, 3 = 2', 3 = 2', 5 = 2', 5 = 2, 9 = 2', 9 = 2, 15 = 3, 15 ~ 1.5; 5, 6 = 6, 7 = 10; 7, 8 ~ 0.7; 7, 13 = 3.5; 7, 13' = 3; 8, 9 = 3; compound **9**: 1, 2 = 1, 2' = 1, 5 = 1, 10 ~ 7.5; 2, 3 ~ 3; 5, 6 = 6, 7 = 10; 7, 8 = 3; 7, 11 = 7; 8, 9 = 5.5; 9, 10 = 7.5; OTig: 3', 4' = 7; 3', 5' = 4', 5' = 1.5.



The IR spectrum of **6** already indicated the presence of a γ -lactone with an acid function and an unsaturated ester group, while the ^1H NMR spectrum (Table 1) showed the presence of a tiglate residue. All signals were close to those of an angelate which was isolated previously from *Grazielia intermedia* [3]. Accordingly, the structure of this acid was clear. Most likely **6** was a precursor of **8**.

The lactones isolated now highly support the placement of the genus *Campovassouria* in the subtribe Disynaphiinae. As mentioned before lactones closely

related to **6** and **8** are present in *Grazielia intermedia* [3] and other β -lactones in *Disynaphia halimifolia* [5] while germacranolides like **1–3** have been isolated from *Disynaphia multicrenulata* [4]. Lactones like **4** and **5** also are present in both genera. *Grazielia*, *Disynaphia* and *Campovassouria* are taxonomically very closely related [1]. *Symphiopappus*, which has been placed in the same subtribe, is not so close to these genera as also follows from the chemistry. So far the kaurene derivatives are replaced by clerodanes and lactones are missing [9].

EXPERIMENTAL

The air dried aerial parts (530 g, voucher RMK 8568) were worked-up in the usual fashion. The polar CC fractions (Et₂O and Et₂O–MeOH, 10:1) afforded by TLC (silica gel, Et₂O–petrol, 3:1) three bands. The least polar one gave by TLC (twice, Et₂O–petrol, 1:1) and HPLC (RP 8, MeOH–H₂O, 13:7) 8 mg **8**. The next band afforded by TLC (silica gel, Et₂O–petrol, 1:1, twice) three zones which were further separated by HPLC (RP 8, MeOH–H₂O, 3:2). The least polar band gave 1 mg **6**, 2 mg **3** and 1 mg **8** (decreasing polarity). HPLC (RP 8, MeOH–H₂O, 3:2) of the next band gave 2 mg **4** and HPLC of the most polar band (RP 8, MeOH–H₂O, 3:2) afforded 1 mg **7** and 1 mg **5** (decreasing polarity). The most polar band of the original TLC afforded by TLC (CHCl₃–C₆H₆–Et₂O, 1:1:1) and HPLC (RP 8, MeOH–H₂O, 11:9) 20 mg **2** and 10 mg **1** (decreasing polarity). Known compounds were identified by comparing the 400 MHz ¹H NMR spectra with those of authentic material. The structure of **7** was established by ¹H NMR spectroscopy and spin decoupling which allowed the assignment of all signals which agreed with those reported in the literature [10]. Compound **6** was homogeneous by TLC and ¹H NMR, but could not be induced to crystallize.

8β-Tigloyloxyguaiaigrazielolide (**8**). Colourless crystals, mp. 217–219°; IR ν_{max}^{CCl₄} cm^{–1}: 1833 (β-lactone), 1770 (γ-lactone), 1720, 1659 (C=CCO₂R); MS *m/z* (rel. int.): 356.126 [M]⁺ (12) (C₂₀H₂₀O₆), 256 [M – RCO₂H]⁺ (6), 212 [256 – CO₂]⁺ (7), 83 [C₄H₇CO]⁺ (100), 55 [83 – CO]⁺ (41).

$$[\alpha]_{24}^D = \frac{589}{-123} \quad \frac{578}{-133} \quad \frac{546}{-153} \quad \frac{436 \text{ nm}}{-300} \quad \text{CHCl}_3; c = 0.03.$$

To 4 mg **8** in 0.5 ml MeOH 10 mg NaBH₄ were added. After 10 min at room temp. dil. H₂SO₄ was added. TLC of the Et₂O extract (Et₂O–petrol, 3:1) gave 2 mg **9**, IR ν_{max}^{CCl₄} cm^{–1}: 1890 (β-

lactone), 1790 (γ-lactone), 1720, 1650 (C=CCO₂R); MS *m/z* (rel. int.): 360.157 [M]⁺ (2) (C₂₀H₂₄O₆), 260 [M – RCO₂H]⁺ (2), 216 [260 – CO₂]⁺ (2), 201 [216 – Me]⁺ (2), 83 [C₄H₇CO]⁺ (100), 55 [83 – CO]⁺ (26).

Desacyl grazielia acid tiglate (**6**). IR ν_{max}^{CCl₄} cm^{–1}: 3500–2600, 1695 (C=CCO₂H), 1780 (γ-lactone), 1730, 1650 (C=CCO₂R); MS *m/z* (rel. int.): 360.157 [M]⁺ (1) (C₂₀H₂₄O₆), 260 [M – RCO₂H]⁺ (6), 242 [260 – H₂O]⁺ (5), 83 [C₄H₇CO]⁺ (100).

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