Table 1. $^1$H NMR spectral data of compound **1** (400 MHz, TMS as internal standard)

| | $C_6D_6$ | $CDCl_3$ |
|---|---|---|
| H-2 | 2.07 *t* | 2.31 *t* |
| H-3 | 1.47 *tt* | 1.61 *tt* |
| H-4 | 1.12 *tt* | 1.41 *m* |
| H-5 | 1.81 *dt* | 2.08 *dt* |
| H-6 | 5.43 *dt* | 5.74 *dt* |
| H-7 | 5.88 *dd* | 6.06 *dd* |
| H-8 | 6.79 *dd* | 6.51 *dd* |
| H-9 | 5.74 *br d* | 5.58 *br d* |
| H-12 | 5.70 *br d* | |
| H-13 | 6.18 *dt* | 6.11 *dt* |
| H-14 | 1.83 *dt* | 2.11 *dt* |
| H-15 | 1.16 *tq* | 1.41 *m* |
| H-16 | 0.74 *t* | 0.88 *t* |
| OMe | 3.38 *s* | 3.66 *s* |

*J* (Hz): 2, 3 = 3, 4 = 4, 5 = 5, 6 = 13, 14 = 14, 15 = 15, 16 ~ 7; 6, 7 = 8, 9 = 12, 13 = 15; 7, 8 = 10.

the latter collapsed the broadened double triplet to a doublet. As this signal was further coupled with the doublet triplet at $\delta$ 6.18, which itself was coupled with a proton adjacent to the triple bond, the positions of the double bonds were established. Similarly the signals of H-2–H-9 could also be assigned. Since the acetylenic ester **2** and **3** had been isolated previously from the same plant, the question arose whether **1** is the precursor of **2** and **3** or formed by hydrogenation of **3** via **2**. So far this point of general interest in the biogenesis of acetylenic compounds is not established though most of these steps were confirmed by feeding experiments [2].

## EXPERIMENTAL

The air-dried aerial parts (30 g) (voucher 81/216, deposited in the Botanic Research Institute, Pretoria) were extracted with $Et_2O$–petrol (1:2) and the resulting extract was separated by TLC (Si gel) using $Et_2O$–petrol (1:10). 4 mg **1** were obtained, colourless gum, IR $\nu_{max}^{CCl_4}$ cm$^{-1}$: 2180 (very weak, C≡C), 1740 ($CO_2R$), 1640, 990, 960 [*trans*, *trans* $(CH{=}CH)_2$ and *trans* CH=CH]; UV $\lambda_{max}^{Et_2O}$ nm: 310, 290, MS *m/z* (rel. int.): 260.178 $[M]^+$ (28 ($C_{17}H_{24}O_2$), 229 $[M-OMe]^+$ (2), 217 $[M-C_3H_7]^+$ (4), 157 $[C_{12}H_{13}]^+$ (21), 143 $[C_{11}H_{11}]^+$ (21), 129 $[C_{10}H_9]^+$ (44), 117 $[C_9H_9]^+$ (100), 91 $[C_7H_7]^+$ (58).

*Acknowledgements*—We thank Dr. B. de Winter and Miss M. Welman, Botanic Research Institute, Pretoria, for their help and the Deutsche Forschungsgemeinschaft for financial support.

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*Phytochemistry*, Vol. 21, No. 11, pp. 2743–2745, 1982.
Printed in Great Britain.

0031-9422/82/112743-03$03.00/0


# SESQUITERPENE LACTONES FROM *INEZIA INTEGRIFOLIA**

FERDINAND BOHLMANN and CHRISTA ZDERO

Institute for Organic Chemistry, Technical University of Berlin, D-1000 Berlin 12, West Germany

(*Received* 21 *December* 1981)

**Key Word Index**—*Inezia integrifolia*; Compositae; sesquiterpene lactones; eudesmanolides; guaianolide.

**Abstract**—*Inezia integrifolia* afforded, in addition to known compounds, three new eudesmanolides and a guaianolide. Two of the eudesmanolides were obtained as a mixture. The relative position of the ester groups could not be determined with certainty. The chemotaxonomy is discussed briefly.

*Inezia* is a monotypic genus placed in the tribe Anthemideae. Morphological data indicated a relationship to *Lidbeckia* and *Thaminophyllum* [1], all three genera being endemic in South Africa. As the chemistry of the latter two genera has been studied [2, 3], it was of interest whether that of *Inezia* supports the proposed relationship. The roots of *I. integrifolia* (Klatt.) Phill. afforded **1** and **2** [4] and nerol isovalerate (**3**), while the aerial parts gave germacrene D, bicyclogermacrene, linoleic and linolenic acids as well as their triglycerides and four sesquiterpene lac-

*Part 451 in the series "Naturally Occurring Terpene Derivatives". For Part 450 see Salam, N. A. A., Mahmoud, Z. F., Ziesche, J. and Bohlmann, F. (1982) *Phytochemistry* **21**, 2746.

Table 1. $^1$H NMR spectral data of compounds **4–6** (400 MHz, $CDCl_3$, TMS as int. standard)

| | **4** | **5** | **6** |
|---|---|---|---|
| H-1 | 5.00 *d br* | 5.10 *br d* | 5.07 *br d* |
| H-2 | 5.07 *ddd* | 5.14 *ddd* | |
| H-3α | 2.50 *br dd** | 2.52 *m* | |
| H-3β | 2.45 *dd** | | |
| H-5 | 2.29 *br d* | 2.29 *br d* | |
| H-6α | 1.83 *ddd* | 1.84 *ddd* | |
| H-6β | 1.42 *dd* | 1.40 *m* | |
| H-7 | 2.99 *br dddd* | 2.98 *br dddd* | |
| H-8 | 4.54 *ddd* | 4.54 *ddd* | |
| H-9α | 1.74 *dd* | 1.74 *dd* | |
| H-9β | 2.00 *dd* | 2.03 *dd* | |
| H-13 | 6.16 *d* | 6.15 *d* | |
| H-13′ | 5.61 *d* | 5.60 *d* | |
| H-14 | 0.98 *s* | 1.02 *s* | 1.00 *s* |
| H-15 | 4.97 *br s* | 4.99 *br s* | |
| H-15′ | 4.66 *br s* | 4.66 *br s* | |
| OCOR | — | 6.07 *qq* | 6.76 *qq* |
| | | 1.97 *dq* | 1.77 *dq* |
| | | 1.81 *dq* | 1.76 *br s* |
| OAc | 2.16 *s* | 2.14 *s* | 2.16 *s* |
| | 1.97 *s* | — | — |

*$C_6D_6$: 2.51 *dddd* (H-3α) and 2.33 *ddd* (H-3β).

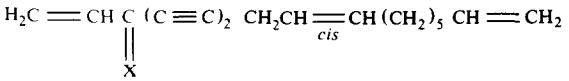
*J*(Hz): 1,2 = 2,5; 2,3α = 11.5; 2,3β = 6.5; 3α,3β = 13; 3α, 15 = 5, 15 ~ 1; 5.6α = 2.5; 5.6β = 12; 6α,6β = 14; 6α,7 = 7; 7,8 = 5; 7.13 = 1; 8,9α = 4; 8,9β = 1.5; 9α,9β = 16; OCOR: 3′,4′ = 7; 3′,5′ = 4′,5′ = 1.

Table 2. $^1$H NMR spectral data of compounds **7** and **8** (400 MHz, $CDCl_3$, TMS as int. standard)

| | **7** | **8** |
|---|---|---|
| H-1 | 1.99 *br dd* | 2.08 *br dd* |
| H-2 | 4.82 *br d* | 4.83 *dd* |
| H-3 | 5.72 *br s* | 5.74 *br s* |
| H-5 | 2.66 *br dd* | 2.62 *br dd* |
| H-6 | 4.34 *dd* | 4.74 *dd* |
| H-7 | 3.30 *dddd* | 3.20 *dddd* |
| H-8 | 5.21 *ddd* | 5.56 *ddd* |
| H-9α | 1.65 *m* | 2.02 *dd* |
| H-9β | 3.25 *br dd* | 2.91 *ddd* |
| H-13 | 6.23 *d* | 6.36 *d* |
| H-13′ | 5.58 *d* | 5.57 *d* |
| H-14 | 2.87 *d* | 2.78 *d* |
| H-14′ | 2.78 *dd* | 2.72 *dd* |
| H-15 | 1.99 *br s* | 2.02 *br s* |
| OTigl | 6.91 *qq* | 6.73 *qq* |
| | 1.84 *dq* | 1.76 *dq* |
| | 1.85 *dq* | 1.73 *dq* |

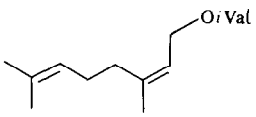
*J* (Hz): 1,2 = 6; 2,3 ~ 2; 1,5 = 8; 3,15 ~ 1; 5,6 = 10.5; 6,7 = 9; 7,8 = 10; 7,13 = 3.5; 7,13′ = 3; 8,9α = 2.5; 8,9β = 5; 9α,9β = 15; 9β,14′ = 1; 14,14′ = 5; OTigl: 3′,4′ = 7; 3′,5′ = 4.5′ = 1.

tones, the isoalantolactone derivatives **4–6** and the guaianolide **7**. The structures followed from the $^1$H NMR spectra. When the spectra of **4–6** (Table 1) were compared, it was obvious that these compounds differed only in the nature of one of the ester residues. While **4** was a diacetate, one acetate group was replaced by an angelate in **5** and by a tiglate in **6**. The latter two compounds could not be separated. The similarity of several signals with those of isoalantolactone (H-5–H-9 and H-15) indicated the presence of diesters of the latter. Careful spin decoupling showed that the ester groups had to be placed at C-1 and C-2, while the couplings indicated that both were α-orientated. Irradiation of the H-2 signal allowed the assignment of the H-3 signals, which partly overlapped in deuteriochloroform, but were nicely separated in deuteriobenzene, thus showing that one of the H-3 protons was allylically coupled to H-15. As already indicated by the chemical shifts of these protons the positions of the ester groups was settled. The relative positions of the angelate and the tiglate, respectively, could not be assigned with certainty as the small amount of material did not allow partial saponification or partial reduction of these diesters. The corresponding $^1$H NMR signals were not conclusive. As the mixture contained different amounts of **5** and **6**, the signals could be assigned. The $^1$H NMR spectral data of **7** (Table 2) were close to those of the tiglate **8**, which was isolated from an *Eupatorium* species [5]. However, the chemical shifts of H-6 and H-8 were typically different and the coupling $J_{7,8}$ was much larger in the spectrum of **7** than in **8**,

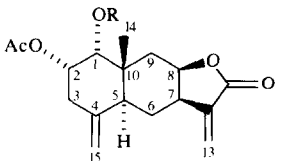


**1** X = O

**2** X = H, OH



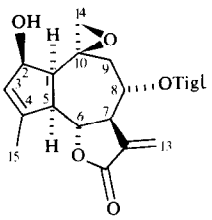
**3**



**4** R = Ac

**5** R = Ang

**6** R = Tigl



**7**

**8** 8β – OTigl

clearly indicating a different stereochemistry at C-8. Therefore **7** was the 8-epimer of **8**. Inspection of a model showed that the couplings observed agreed with the angles. The *W*-coupling $J_{9,14}$ indicated a 10β-orientated epoxy group. The chemistry of *Inezia* shows relationships to *Lidbeckia* [2] and *Thaminophyllum* [3] by the co-occurrence of acetylenes of type **1** and to *Lidbeckia* by the isolation of a guaianolide, thus supporting the proposed close affinity of these genera.

## EXPERIMENTAL

The air-dried plant material, collected in Transvaal in Feb. 1981 (voucher 81/140, deposited in the Botanic Research Institute, Pretoria) was extracted with $Et_2O$–petrol (1:2), and the resulting extracts were separated by CC (Si gel) and further by repeated TLC (Si gel). The roots (120 g) afforded 5 mg **1**, 5 mg **2** and 5 mg **3**, while the aerial parts (50 g) gave 3 mg germacrene D, 1 mg bicyclogermacrene, 50 mg of a mixture of linoleic and linolenic acids, 20 mg of their triglycerides, 3 mg **4**, 0.7 mg **5**, 1.2 mg **6** and 1 mg **7** (lactones separated by TLC with $Et_2O$–petrol, 3:1 and then $C_6H_6$–$CHCl_3$–$Et_2O$, 2:2:1).

*1α,2α-Diacetoxy-isoalantolactone* (**4**). Colourless gum, IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 1780 (γ-lactone), 1755, 1250 (OAc); MS *m/z* (rel. int.): 288.136 $[M-HOAc]^+$ (5) ($C_{17}H_{20}O_4$), 246 [288 – ketene]$^+$ (33), 228 $[288-HOAc]^+$ (100), 213 $[228-Me]^+$ (29);

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+68 \quad +68 \quad +75 \quad +125} \quad (CHCl_3;\ c\ 0.11).$$

*1α- or 2α-Angeloyloxy- and tigloyloxy esters of 1α- or 2α-acetoxy-isoalantolactone* (**5** *and* **6**). Colourless gum, which could not be separated, IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 1775 (γ-lactone), 1750, 1250 (OAc), 1720 (C=$CCO_2R$); MS *m/z* (rel. int.): 388.189 $[M]^+$ (0.4) ($C_{22}H_{28}O_6$), 328 $[M-HOAc]^+$ (0.4), 289 $[M-OCOR]^+$ (1.2), 288 $[M-HO_2R]^+$ (1.6), 246 [288 – ketene]$^+$ (5), 228 $[288-HOAc]^+$ (15), 83 $[C_4H_7CO]^+$ (43).

*8α-Tigloyloxypre-eupatundin-10β, 14-epoxide* (**7**). Colourless gum, IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 3600 (OH), 1780 (γ-lactone), 1715, 1650 (C=$CCO_2R$); MS *m/z* (rel. int.): 260.105 $[M-HO_2CR]^+$ (2) ($C_{15}H_{16}O_4$), 242 $[260-H_2O]^+$ (4), 227 $[242-Me]^+$ (4), 83 $[C_4H_7CO]^+$ (100), 55 $[83-CO]^+$ (72).

*Acknowledgements*—We thank Dr. B. de Winter and Miss M. Welman, Botanic Research Institute, Pretoria, for their help during plant collection and identification of the plant material and the Deutsche Forschungsgemeinschaft for financial support.

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