*Phytochemistry*, Vol. 21, No. 5, pp. 1153–1154, 1982.
Printed in Great Britain.

0031–9422/82/051153–02$03.00/0

# 11-HYDROXY-α- AND β-CUBEBENE FROM *EUPATORIUM SEROTINUM**

FERDINAND BOHLMANN, JASMIN JAKUPOVIC and WOLFGANG VOGEL

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

(*Received* 9 *September* 1981)

**Key Word Index**—*Eupatorium serotinum*; Compositae; sesquiterpenes; cubebene derivatives.

**Abstract**—The aerial parts of *Eupatorium serotinum* contain 11-hydroxy-α- and β-cubebene.

A re-investigation of the less polar fractions from the aerial parts of *Eupatorium serotinum* Michx. afforded in addition to germacrene D, α-humulene, β-cubebene, and stigmasterol three sesquiterpene alcohols. All three had the molecular formula $C_{15}H_{24}O$. One of these compounds, the cadinene derivative **2** has been previously isolated from a *Hemizonia* species [1]. This species also contained 11-hydroxycubebol, its $^1H$ NMR spectrum and that of cubebene in parts were similar to those of the two remaining alcohols (Table 1), which were the corresponding isomeric anhydro derivatives **3** and **4**. In deuteriobenzene at 400 MHz all signals of **3** could be assigned by spin decoupling. Starting with the triplet at 1.24 ppm, obviously due to a cyclopropane proton, the sequence H-5 through H-10 (H-14) could be established, while the presence

Table 1. $^1H$ NMR spectral data of compounds **3** and **4** (400 MHz, TMS as int. standard)

| | **3** ($C_6D_6$) | Δ‡ | **4** ($CDCl_3$) | **3** | $^{13}C$ ($CDCl_3$) | Δ* |
|---|---|---|---|---|---|---|
| H-2α | 2.00 *ddd*† | 0.2 | 2.53 *br d* | C-1 | 37.9 *s* | 1.5 |
| H-2β | 2.15 *br*† *dd* | 0.15 | 2.16 *br d* | C-2 | 26.1 *t* | 1.4 |
| H-3α | 2.09 *br dddd* | 0.25 | 4.91 *br s* | C-3 | 30.3 *t* | 1.4 |
| H-3β | 1.53 *m*† | 0.47 | | C-4 | 154.6 *s* | 0.8 |
| H-5α | 1.47 *d* | 0.63 | 1.20§ | C-5 | 31.5 *d* | 0.7 |
| H-5β | 1.24 *t* | 1.76 | 0.37 *dd* | C-6 | 26.1 *d* | 1.4 |
| H-7α | 1.23 *ddd* | 2.21 | 1.2 *m* | C-7 | 49.4 *d* | 4.9 |
| H-8α | 1.47 *brd* | 1.51 | 1.5 *m* | C-8 | 29.4 *t* | 4.3 |
| H-8β | 0.88 *dddd* | 1.02 | 0.85 *m* | C-9 | 30.3 *t* | 2.5 |
| H-9α | 0.55 *dddd* | 0.54 | 0.54 *dddd* | C-10 | 35.9 *d* | 1.5 |
| H-9β | 1.58 *br d* | 0.32 | 1.5 *m* | C-11 | 73.1 *s* | 10.8 |
| H-10β | 1.75 *ddq* | 0.50 | 1.75 *m* | C-12 | 27.6 *q* | 4.3 |
| H-12 | 1.16 *s* | 2.12 | 1.24 *s* | C-13 | 26.7 *q* | 2.4 |
| H-13 | | 2.01 | 1.20 *s* | C-14 | 18.8 *q* | 0.5 |
| H-14 | 1.03 *d* | 0.13 | 0.93 *d* | C-15 | 101.5 *t* | 0.6 |
| H-15 | 5.07 *ddd* | 0.12 | 1.75 *ddd* | | | |
| H-15′ | 4.84 *ddd* | 0.05 | | | | |

*Δ-values after addition of $Yd(fod)_3$.

†Not first order.

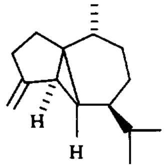
‡Δ-values after addition of $Eu(fod)_3$.

§Overlapped.

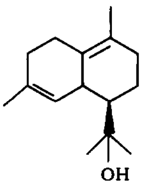
*J*(Hz): Compound **3**: 2α, 2β ~ 12; 2α, 3α ~ 9; 2α, 3β ~ 10; 2β, 3α ~ 8; 3α, 3β ~ 13; 3α, 15 = 2; 5α, 6β = 2.5; 6β, 7α ~ 2.5; 7α, 8α ~ 3.5; 7α, 8β = 8α, 8β = 8β, 9α = 12; 8α, 9α = 8β, 9β = 2; 9α, 9β = 13; 9α, 10β = 12; 9β, 10β = 10β, 14 = 6.5; 15, 15′ = 1; compound **4**: 2α, 2β = 16; 2, 15 = 5, 15 ~ 2; 5,6 = 2.5; 7,8β = 8α,8β = 8β,9α = 12; 8α,9α = 8β,9β = 2; 9α,9β = 13; 9α,10β = 12; 10β, 14 = 6.5.

---

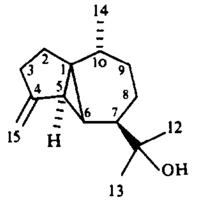
*Part 423 in the series "Naturally Occurring Terpene Derivatives". For Part 422 see Bohlmann, F., Zdero, C. and Ahmed, M. (1982) *Phytochemistry*, **21**, (in press).



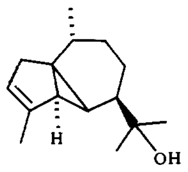
1



2



3



4

of an exo-methylene, a secondary methyl and dimethyl carbinol group followed from the remaining signals. Structure **3** was further supported by the $^{13}C$ NMR spectrum (Table 1). Also the observed shifts in the $^{1}H$ and $^{13}C$ NMR spectra after addition of shift reagent supported the assignments. The $^{1}H$ NMR spectrum of **4** differed from the typical spectrum of **3**, the exomethylene signals being replaced by an olefinic methyl and an olefinic proton signal. Although the remaining signals were similar to those of **3**, several chemical shifts were different. In particular, that of H-6 was at a higher field in the spectrum of **4**. Obviously in compound **3** this proton was deshielded by the exo-methylene double bond. As the couplings observed in the spectra of **3** and **4** were nearly the same as those of **1** and 11-hydroxycubebol, identical stereochemistry at the asymmetric centres can be proposed. **1–4** are clearly biogenetically related. Although cubebene derivatives so far seem to be rare in Compositae, their co-occurrence in unrelated tribes indicates that they may not be of chemotaxonomic importance. From the same species, however, typical highly oxygenated germacranolides were isolated [2].

## EXPERIMENTAL

The air-dried aerial parts (500 g) (voucher LeVan 78/32) were extracted with $Et_2O$–petrol (1:2) and the resulting extract separated by CC (Si gel) and further by TLC (Si gel). The non-polar fractions (petrol) afforded 30 mg germacrene D, 30 mg $\alpha$-humulene and 20 mg $\beta$-cubebene, while the fractions with petrol–$Et_2O$, (1:3 gave 10 mg stigmasterol, 10 mg **2**, 50 mg **3** and 20 mg **4** on repeated TLC ($Et_2O$–petrol, 3:1).

*11-Hydroxy-$\beta$-cubebene* (**3**). Colourless crystals, mp 85° (petrol), $IR\nu_{max}^{CCl_4}$, $cm^{-1}$: 3620 (OH), 1650, 875 ($C{=}CH_2$); MS *m/z* (rel. int.): 220.183 $[M]^+$ (0.3) ($C_{15}H_{24}O$), 202 $[M-H_2O]^+$ (20), 162 $[M-Me_2C{=}O]^+$ (85), 147 $[162-Me]^+$ (60), 59 $[Me_2COH]^+$ 100-.

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589}{-44}\quad\frac{578}{-45}\quad\frac{546}{-51}\quad\frac{436\,\text{nm}}{-72}\quad (CHCl_3;\ c\ 1.35).$$

*11-Hydroxy-$\alpha$-cubebene* (**4**). Colourless oil, $bp_{0.1}$ 150°, $IR\nu_{max}^{CCl_4}$ $cm^{-1}$: 3620 (OH), 1650 (C=C); MS *m/z* (rel. int.): 220. 183 $[M]^+$ (0.5), 202 $[M-H_2O]^+$ (12), 162 $[M-Me_2CO]^+$ (80), 59$[Me_2COH]^+$ (100).

*Acknowledgements*—We thank Dr. N. Le Van for the plant material and the Deutsche Forschungsgemeinschaft for financial support.

## REFERENCES

1. Bohlmann, F., Jakupovic, J., Ahmed, M., Wallmeyer, M., Robinson, H. and King, R. M. (1981) *Phytochemistry* **20**, 2383.
2. Herz, W., deGroote, A., Murari, R. and Kumar, N. (1979) *J. Org. Chem.* **44**, 2784.