Phytochemistry, Vol. 21, No. 7, pp. 1795–1797, 1982.
Printed in Great Britain.

0031-9422/82/071795-03$03.00/0

EUDESMANE DERIVATIVES FROM *EPALTES BRASILIENSIS**

FERDINAND BOHLMANN, NALEEN BORTHAKUR, HAROLD ROBINSON† and ROBERT M. KING†

Institute for Organic Chemistry, Technical University of Berlin, D-1000 Berlin 12, West Germany; †Smithsonian Institution, Department of Botany, Stop No. 166, Washington, DC 20560, U.S.A.

(*Received* 18 *August* 1981)

Key Word Index—*Epaltes brasiliensis*; Compositae; Inuleae; sesquiterpenes; eudesmane derivatives; dithiophene acetylene.

Abstract—The first investigation of an *Epaltes* species afforded two thiophene acetylenes and several eudesmane derivatives, all closely related to cuauhtemone, its esters being typical for *Pluchea* species. The structures were elucidated by spectroscopic methods.

INTRODUCTION

So far nothing is known of the chemistry of the genus *Epaltes* (Compositae), which is placed in the subtribe Inulinae (tribe Inuleae) in the *Pluchea* group [1]. We have now studied the constituents of *E. brasiliensis* DC. to determine whether the chemistry shows any relationships to that of *Pluchea*.

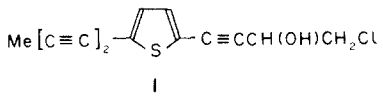
The roots afforded, in addition to stigmasterol, the thiophene chlorohydrins **1** [2] and **2**. The structure of the latter compound followed from the spectroscopic data. The UV spectrum showed broad maxima at 340 and 328 nm typical for a dithiophene acetylene. The molecular formula of $C_{13}H_{11}OClS$ was deduced from the mass spectrum. The base peak was formed by loss of CH_2Cl indicating a terminal chloromethyl group. The ^{1}H NMR spectrum (see Experimental) displayed typical thiophene doublets characteristic of 2,5′-disubstituted dithiophenes, while spin decoupling showed that a broad multiplet at δ5.14 was coupled with two double doublets at δ3.76 and 3.84. Furthermore the diol **3** was obtained, its structure followed from the molecular formula and the ^{1}H NMR spectrum (Table 1). All the signals could not be interpreted, but the characteristic ones clearly indicated the presence of a eudesmane derivative. The nature of the oxygen functions followed from the doublets at δ3.57 and 3.43 and from the methyl signals. Accordingly the ^{1}H NMR spectrum was similar to that of 11-hydroxy-dihydrocostol [3]. The last compound, the ketone **8**, was also present in the aerial parts which afforded in addition to taraxasteryl acetate and stigmasterol five eudesmane derivatives, all closely related to cuauhtemone [4]. Careful ^{1}H NMR studies led to the structures **4–8** (Table 1). The molecular formula was $C_{22}H_{34}O_6$ for both **4** and **5**, indicating they were isomers. Also the ^{1}H NMR spectra were nearly identical. However, some chemical shifts were slightly different. In particular, the shifts of an olefinic proton at δ7.10 and 6.83 respectively, which most likely were to be those of H-6, indicated a difference in the stereochemistry at C-4. Obviously there was deshielding of H-6 by the 4α-acetoxy group as could be deduced from a model, which further showed that a *trans*-fused decalin should be proposed, if the coupling $J_{5,6}$ was considered. Also small differences were observed in the chemical shifts of H-14 and the acetoxy methyl. The position of the hydroxyl at C-11 only followed indirectly from the downfield shift of the corresponding methyl signals and from the shifts of H-6, which were unusual for a simple conjugated ketone. The relative position of the ester groups was assigned only by analogy, as this type is typical for cuauhtemone diesters [4–7]. Partial hydrolysis to establish this arrangement was unsuccessful. The stereochemistry at C-3 followed from the couplings $J_{2,3}$. Compounds **4** and **5** therefore were Δ^6-isomeric hydroxylated 3-epi-cuauhtemones. The ^{1}H NMR spectrum of compound **6** differed in some details from that of **4**, as the acetate group was missing. As in other esters of this type [7] this caused a drastic upfield shift of the signal of H-3. The H-6 signal again was at very low fields, indicating a 4α-hydroxy group. The ^{1}H NMR data of **4** and **6** are very similar to those of the corresponding angelates [7], which further supported the proposed structures. The structures of **7** and **8** clearly followed from the ^{1}H NMR data, which again were close to those of the corresponding angelate from *Pluchea odorata* [5]. The stereochemistry at C-4 followed from the downfield shift of the H-6 signal, while that at C-3 was deduced from the couplings $J_{2,3}$. Compounds **7** and **8** therefore are further esters of cuauhtemone.

*Part 417 in the series "Naturally Occurring Terpene Derivatives". For Part 416 see Bohlmann, F., Wallmeyer, M., King, R. M. and Robinson, H. (1982) *Phytochemistry* **21**, 1439.

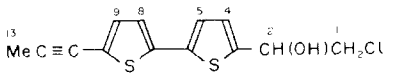
Table 1. ^{1}H NMR spectral data of compounds **3–8** (400 MHz, $CDCl_3$, TMS as int. standard)

	3	4	5	6	7	8
H-3	—	5.98 *dd*	5.95 *dd*	4.81 *dd*	4.75 *dd*	5.83 *dd*
H-4	1.42 *m*	—	—	—	—	—
H-5	2.0 *m*	4.08 *d*	4.03 *d*	2.61 *d*	—	—
H-6	2.27 *br dd* 3.13 *ddd*	7.10 *d*	6.83 *d*	7.23 *d*	3.05 *br dd* 2.38 *dd*	3.16 *dd* 2.27 *m*
H-8	5.33 *ddd*	—	—	—	—	—
H-9α	2.03 *m*	2.31 *d*	2.31 *d*	2.28 *d*	2.19 *br d*	2.17 *d*
H-9β	1.93 *br d*	2.38 *d*	2.37 *d*	2.34 *d*	2.26 *d*	2.24 *d*
H-12	3.57 *d* 3.43 *d*	1.53 *s*	1.41 *s*	1.52 *s*	2.04 *d*	1.97 *d*
H-13	1.09 *s*	1.47 *s*	1.44 *s*	1.49 *s*	1.86 *d*	1.76 *d*
H-14	0.94 *s*	1.02 *s*	0.97 *s*	0.99 *s*	0.98 *s*	0.96 *s*
H-15	0.88 *d*	1.39 *s*	1.33 *s*	1.24 *s*	1.24 *s*	1.35 *s*
OCOR	—	2.44 *tq* 1.69 *ddq* 1.50 *ddq* 0.96 *t* 1.20 *d*	2.40 *tq* 1.67 *ddq* 1.50 *ddq* 0.92 *t* 1.16 *d*	2.44 *tq* 1.68 *ddq* 1.50 *m* 0.96 *t* 1.21 *d*	2.44 *tq* 1.69 *ddq* 1.5 *ddq* 0.96 *t* 1.20 *d*	2.37 *tq* 1.63 *ddq* 1.47 *ddq* 0.95 *t* 1.15 *d*
OAc	—	2.02 *s*	1.97 *s*	—	—	1.93 *s*
OH	—	7.96 *br s*	—	8.14 *br s*	—	—

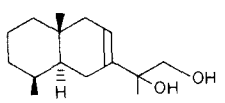
J (Hz): Compound **3**: 4, 15 = 7; 5,6 = 12; 5,6′ = 4; 6,6′ = 14; 6,8 = 2; 8,9α ~ 2; 8,9β ~ 5; 9α9β ~ 15; 12,12′ = 11; compounds **4–6**: 2α,3 = 4.5; 2β,3 = 11; 5,6 = 2; 9α,9β = 15; compounds **7** and **8**: 2α,3 = 5; 2β,3 = 11; 5,6 = 4; 6,6′ = 13; 6′,12 = 1.5; 6′,13 = 1; 9α,9β = 15; OMeBu: 2′,3′ = 2′,5′ = 3′,4′ = 7; 2′,2′ = 14.



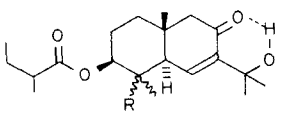
1



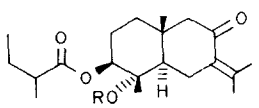
2



3



4 R = αOAc
5 R = βOAc
6 R = αOH



7 R = H
8 R = Ac

The chemistry of this *Epaltes* species showed a close relationship to that of *Pluchea*, where cuauhtemone derivatives are widespread. The placement of *Epaltes* in the *Pluchea* group of the subtribe Inulinae therefore also is supported by the constituents.

EXPERIMENTAL

The air-dried plant material, collected in north-eastern Brazil (voucher RMK 8684, deposited in the U.S. National Herbarium, Washington) was extracted with Et_2O–petrol (1 : 2) and the resulting extracts were separated first by CC (Si gel) and further by repeated TLC (Si gel). The roots (50 g) afforded 10 mg stigmasterol, 0.5 mg **1**, 1 mg **2** ($AgNO_3$-coated Si gel, Et_2O–petrol, 1:2), 21 mg **3** (Et_2O-CH_2Cl_2–MeOH, 10 : 40 : 1) and 2 mg **4** (Et_2O–CH_2Cl_2, 1 : 4), while the aerial parts (300 g) gave 20 mg stigmasterol, 20 mg taraxasteryl acetate, 1 mg **4**, 1.7 mg **5** (Et_2O–CH_2Cl_2, 1 : 3), 3.5 mg **6** (Et_2O–CH_2Cl_2, 1 : 4), 20 mg **7** (Et_2O–CH_2Cl_2, 1 : 4) and 9 mg **8** (Et_2O–CH_2Cl_2, 1 : 4).

2-Prop-1-inyl-5′-(2-hydroxy-3-chloropropyl) dithiophene (**2**). Colourless gum, UV $\lambda_{max}^{Et_2O}$, nm: 340, 328; MS *m/z* (rel. int.): 282 $[M]^+$ (34), 264 $[M-H_2O]^+$ (1), 246 $[M-HCl]^+$ (10), 233.010 $[M-CH_2Cl]^+$ (100) ($C_{12}H_9OC_2$); ^{1}H NMR ($CDCl_3$): δ3.84 (*dd*, *J* = 11.5, 4 Hz, H-1), 3.76 (*dd*, *J* = 11.5, 8 Hz, H-1′), 5.14 (*m*, H-2), 6.96 (*d*, *J* = 4 Hz, H-5), 6.99 (*d*, *J* = 4 Hz, H-9), 7.01 (*d*, *J* = 4 Hz, H-4), 7.03 (*d*, *J* = 4 Hz, H-8), 7.05 (*d*, *J* = 4 Hz), 2.11 (*s*, H-13).

11,12-*Dihydroxyeudesm-7-ene* (**3**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3460 (OH), 1440, 1385, 1350, 1130; MS *m/z* (rel. int.): 238.193 $[M]^+$ (1) ($C_{15}H_{26}O_2$), 220 $[M-H_2O]^+$ (42), 205 $[220-Me]^+$ (21), 202 $[220-H_2O]^+$ (21), 189 $[220-CH_2OH]^+$ (38), 161 $[C_{12}H_{17}]^+$ (100). $[\alpha]_D = +8$ ($CHCl_3$, *c* 2.0).

4*α-Acetoxy*-3*β*-(2-*methylbutyryloxy*)-9′-*hydroxyeudesm*-6-*en*-8-*one* (**4**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3540 (OH), 1740, 1240 (OAc), 1740 (CO_2R), 1670 (C=CC=O); MS *m/z* (rel. int.): 334.214 $[M-HOAC]^+$ (1) ($C_{20}H_{30}O_4$), 319 $[334-Me]^+$ (12), 232 $[334-RCO_2H]^+$ (20), 217 $[232-Me]^+$ (8), 85 $[C_4H_9CO]^+$ (44), 57 $[85-CO]^+$ (100). $[\alpha]_D = -414°$ ($CHCl_3$, *c* 0.1).

4*α*, 11-*Dihydroxy*-3*β*-(2-*methylbutyryloxy*)-*eudesm*-6-*en*-8-*one* (**5**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3420 (OH), 1735 (CO_2R), 1670 (C=CCO); MS *m/z* (rel. int.): 352 $[M]^+$ (0.1), 337.202 $[M-Me]^+$ (20) ($C_{19}H_{29}O_5$), 319 $[337-H_2O]^+$ (1), 235 $[337-RCO_2H]^+$ (7), 85 $[C_4H_9CO]^+$ (49), 57 $[85-CO]^+$ (100).

4*β-Acetoxy*-11-*hydroxy*-3*β*-(2-*methylbutyryloxy*)-*eudesm*-6-*en*-8-*one* (**6**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3540 (OH), 1745, 1245 (OAc), 1745 (CO_2R), 1670 (C=CO=O); MS *m/z* (rel. int.): 334.214 $[M-HOAc]^+$ (3) ($C_{20}H_{30}O_4$), 319 $[334-Me]^+$ (22), 232 $[334-RCO_2H]^+$ (24), 217 $[232-Me]^+$ (10), 85 $[C_4H_9CO]^+$ (52), 57 $[85-CO]^+$ (100). $[\alpha]_D = +4.3°$ ($CHCl_3$, *c* 0.35).

3-O-(2-*Methylbutyryl*)-3-*epi-cuauhtemone* (7). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}. 3500 (OH), 1745 (CO_2R), 1685 (C=CC=O); MS *m/z* (rel. int.): 336.230 $[M]^+$ (8) ($C_{20}H_{32}O_4$), 234 $[M-RCO_2H]^+$ (5), 216 $[234-H_2O]^+$ (7), 85 $[C_4H_9CO]^+$ (42), 57 $[85-CO]^+$ (100). $[\alpha]_D = +20°$ ($CHCl_3$, *c* 0.87).

4-O-*Acetyl*-3-O-(2-*methylbutyryl*)-3-*epi-cuauhtemone* (**8**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3500 (OH), 1740, 1245 (OAc), 1740 (CO_2R), 1675 (C=CC=O); MS *m/z* (rel. int.): 318.214 $[M-HOAc]^+$ (68) ($C_{20}H_{30}O_3$), 216 $[318-RCO_2H]^+$ (82), 201 $[216-Me]^+$ (75), 85 $[C_4H_9CO]^+$ (65), 57 $[85-CO]^+$ (100). $[\alpha]_D = +40°$ ($CHCl_3$, *c* 2.0).

Acknowledgements—We thank Drs. Scott A. Mori and P. Alvim, Herbario Centro de Pesquisas do Cacau at Itabanu, Bahia, Brazil, for their help during plant collection and the Deutsche Forschungsgemeinschaft for financial support.

REFERENCES

1. Merxmüller, H., Leins, P. and Roessler, H. (1977) in *The Biology and Chemistry of the Compositae* (Heywood, V. H., Harborne, J. B. and Turner, B. L., eds.) p. 577. Academic Press, London.
2. Bohlmann, F., Burkhardt, T. and Zdero, C. (1973) *Naturally Occurring Acetylenes*, p. 63. Academic Press, London.
3. Bohlmann, F. and Jakupovic, J. (1979) *Phytochemistry* **18**, 1189.
4. Nakanishi, K., Crouch, R., Miura, I., Dominguez, X. and Zamudio, A. (1974) *J. Am. Chem. Soc.* **96**, 609.
5. Bohlmann, F. and Zdero, C. (1976) *Chem. Ber.* **109**, 2653.
6. Bohlmann, F. and Mahanta, P. K. (1978) *Phytochemistry* **17**, 1189.
7. Bohlmann, F., Ziesche, J., King, R. M. and Robinson, H. (1980) *Phytochemistry* **19**, 969.