Phytochemistry, Vol. 26, No. 5, pp. 1536–1538, 1987.
Printed in Great Britain.

0031–9422/87 $3.00 + 0.00
Pergamon Journals Ltd.

MALABARICANE DERIVATIVES FROM *PYRETHRUM SANTOLINOIDES*

J. JAKUPOVIC, F. EID, F. BOHLMANN and S. EL-DAHMY

Institute for Organic Chemistry, Technical University of Berlin, D-1000 Berlin 12, F.R.G.

(*Received* 7 *July* 1986)

Key Word Index—*Pyrethrum santolinoides*; Compositae; triterpenes; malabaricane derivatives; sesquiterpenes; davanone derivative; carvotanacetone derivatives.

Abstract—The roots of *Pyrethrum santolinoides* afforded two further representatives of the rare type of malabaricane-triterpenes, a davanone derivative and in addition to known compounds a diester derived from carvotanacetone.

The roots of *Pyrethrum santolinoides* DC (= *Tanacetum sinaicum* Del. ex DC) have not been studied chemically. In addition to thymol, *p*-hydroxyacetophenone, stigmasterol, sitosterol, the germacranolide artabin [1], the dimeric coniferyl alcohol derivative **5** [2], davanone [3], the corresponding hydroxy derivative **3**, the carvotanacetone derivative **4** and two triterpenes, the ketone **1** and the acetate **2** were isolated. The structure of **3** directly followed from the ^{1}H NMR spectrum which was identical with that of the product obtained from triphenylphosphine reduction of the corresponding hydroperoxide [4, 5]. The ^{1}H NMR spectrum of **4** which also was transformed to the acetate **4a**, indicated the presence of a carvotanacetone derivative with an acetoxy and a tigloxy group. The position of the free hydroxy group clearly followed from the downfield shift of the H-7 signal in the spectrum of the acetate. Spin decoupling allowed the assignment of all signals and the observed couplings led to the proposed stereochemistry. The relative position of the ester groups was supported by the mass spectrum. Inspection of a model indicated that a *cis*-elimination is only likely with a 3-acyloxy group. The mass spectrum showed elimination of acetic acid and not of tiglic acid. Therefore, a 3-acetoxy derivative is very likely.

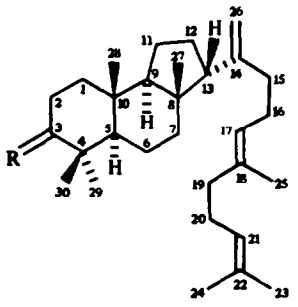
The structures of **1** and **2** followed from the spectral data. The molecular formula of **2** was $C_{32}H_{52}O_2$. Loss of acetic acid led to *m/z* 408 followed by loss of C_5H_9, $C_{10}H_{18}$ and $C_{15}H_{24}$ (*m/z* 339, 270 and 204). The latter fragment is probably formed by splitting the allylic 8,13-bond followed by elimination of the β-farnesene moiety. In agreement with the ^{1}H NMR spectrum (see Experimental) therefore a geranyl and part of a farnesyl derived side chain, respectively, were very likely. The ^{1}H NMR and the ^{13}C NMR spectra further showed that a triterpene of the rare malabaricane series [6, 7] could be present. Spin decoupling and NOE difference spectroscopy established this proposal. Clear NOEs were observed between H-5 and H-3, between H-29 and H-3, between H-27, H-28 and H-13, between H-23 and H-21 as well as between H-19 and H-17. Inspection of models indicated that these effects required the proposed structure and stereochemistry. The ^{13}C NMR data also supported this structure (see Experimental) as the observed chemical shifts nicely agreed with those of compounds which have similar partial structures. The spectral data of compound **1** indicated that only the acetoxy group was replaced by a keto group. If the already proposed name for this rare carbon skeleton is used [6] the ketone **1** is 3-oxo-malabarica-14(26),17*E*,21-triene which most likely is the precursor of malabaricol (**6**) isolated from an *Ailanthus* species [6] where the stereochemistry was established by X-ray analysis [7]. Epoxidation of the Δ^{17}-double bond of **1** would lead to **1a** which by proton attack at C-26 and hydrolysis of the epoxide would give by addition of the secondary hydroxy group at C-14 the natural compound **6** (Scheme 1).

EXPERIMENTAL

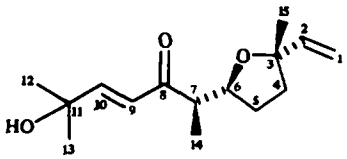
The roots of *Pyrethrum santolinoides* were collected in March 1986 on the Sinai peninsula. The extract (700 mg) obtained with MeOH–Et_2O–petrol (1:1:1) was first separated by CC (silica gel) affording four fractions (Fr. 1: Et_2O–petrol, 1:9; Fr. 2: Et_2O–petrol, 1:4; Fr. 3: Et_2O–petrol, 1:1; and Fr. 4: Et_2O). Prep. TLC (silica gel, PF_{254}) of fraction 1 (Et_2O–petrol, 1:19, two developments) gave 35 mg thymol, 11 mg davanone, 10 mg **2** (R_f 0.4) and 4 mg **1** (R_f 0.5). Prep. TLC of fraction 2 (Et_2O–petrol, 1:3) gave 25 mg thymol, 5 mg davanone and 6 mg **3** (R_f 0.6). Prep. TLC of fraction 3 (Et_2O–petrol, 1:3, two developments) gave 30 mg stigmasterol, 20 mg sitosterol, 20 mg *p*-hydroxyacetophenone and 15 mg **5**. Prep. TLC of fraction 4 (Et_2O–C_6H_6–CH_2Cl_2, 1:5:5, two developments) gave 7 mg **4** and 3 mg artabin. Known compounds were identified by comparing the 400 MHz ^{1}H NMR spectra with those of authentic material.

3-Oxo-malabarica-14(26),17E,21-triene (**1**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1730 (C=O), 1630 (C=C); MS *m/z* (rel. int.): 424.370 [M]$^+$ (4.5) (calc. for $C_{30}H_{48}O$: 424.370), 409 [M – Me]$^+$ (2), 355 [M – C_5H_9]$^+$ (1), 149 (100); ^{1}H NMR ($CDCl_3$): δ0.98, 1.03, 1.05, 1.07 (*s*, H-27–H-30), 1.69 (*br s*, H-23), 1.60 (*br s*, H-24, H-25), 5.13 and 5.10 (*br t*, H-17 and H-21), 4.89 and 4.57 (*br s*, H-26).

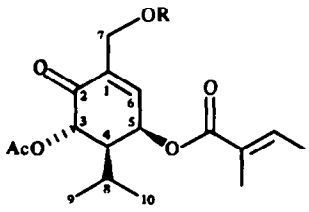
3β-Acetoxymalabarican-14(26),17E,21-triene (**2**). Colourless crystals, mp. 56°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1750, 1260 (OAc), 1630 (C=C), 3080, 910 (C=CH_2); MS *m/z* (rel. int.): 468.397 [M]$^+$ (2) (calc. for $C_{32}H_{52}O_2$: 468.397), 408 [M – HOAc]$^+$ (0.7), 339 [408



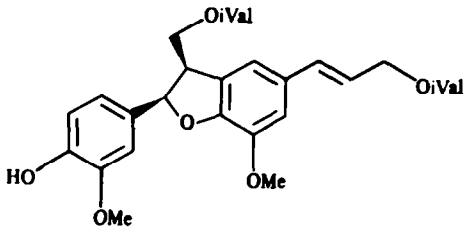
1 R = O
2 R = βOAc,H



3



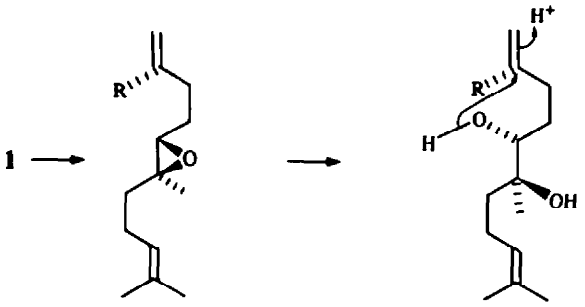
4 R = H
4a R = Ac



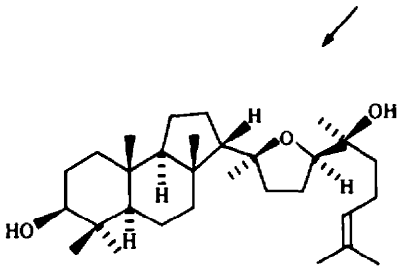
5

$-C_5H_9]^+$ (1.7), 270 [408 $-C_{10}H_{18}]^+$ (9), 204 [408 $-C_{15}H_{24}]^+$ (24), 69 $[C_5H_9]^+$ (100); ^{1}H NMR ($CDCl_3$): δ 1.64 (*m*, H-2), 4.78 (*t*, H-3), 0.78 (*dd*, H-5), 1.50 and 1.44 (*m*, H-6), 2.12 (*br d*, H-13), 1.98 (*m*, H-15, H-19), 2.04 (*m*, H-16, H-20), 5.11 (*br t*, H-17), 5.09 (*br t*, H-21), 1.69 (*br s*, H-23), 1.60 (*br s*, H-24, H-25), 4.87 and 4.58 (*br s*, H-26), 0.98 (*s*, H-27), 0.88 (*s*, H-28), 0.84 (*s*, H-29), 0.86 (*s*, H-30) [*J*(Hz): 2,3 = 8.5; 2',3 = 7; 5,6 = 12; 5,6' = 2; 12,13 = 8; 12',13 ~ 1.5; 16,17 = 20,21 = 7]; ^{13}C NMR ($CDCl_3$, C-1–C-30): δ 36.4 *t*, 23.6 *t*, 81.1 *d*, 36.4 *s*, 55.2 *d*, 20.7 *t*, 27.6 *t*, 45.2 *s*, 55.8 *d*, 37.7 *s*, 18.9 *t*, 38.3 *t*, 56.3 *d*, 154.2 *s*, 39.2 *t*, 26.8 *t*, 124.4 *d*, 131.2 *s*, 39.7 *t*, 26.9 *t*, 124.2 *d*, 135.1 *s*, 25.7 *q*, 17.7 *q*, 16.4 *q*, 108.3 *t*, 24.7 *q*, 15.7 *q*, 28.0 *q*, 15.7 *q*; OAc: 170.9 *s*, 21.3 *q* (a few signals may be interchangeable); $[\alpha]_D^{24°}$ + 14 ($CHCl_3$; *c* 1.0).

3α-Acetoxy-7-hydroxy-5β-tigloxy-carvotanacetone (**4**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3590 (OH), 1740, 1245 (OAc), 1730, 1655 (C=CCO$_2$R), 1700 (C=O); MS *m/z* (rel. int.): 324 $[M]^+$ (0.1), 264.136 $[M - HOAc]^+$ (2.5) (calc. for $C_{15}H_{20}O_4$: 264.136), 164 $[264 - RCO_2H]^+$ (12), 83 $[C_4H_7CO]^+$ (100), 55 $[83 - CO]^+$ (64); ^{1}H NMR ($CDCl_3$): δ 5.82 (*d*, H-3), 2.46 (*ddd*, H-4), 5.65 (*dd*, H-5), 6.95 (*br d*, H-6), 4.34 and 4.29 (*br d*, H-7), 2.04 (*dqq*, H-8), 1.04 (*d*, H-9), 0.99 (*d*, H-10), 2.10 (*s*, OAc); OTigl: 6.98 (*br q*), 1.83 (*dq*), 1.90 (*br s*) [*J* (Hz): 3,4 = 12; 4,5 = 4,8 = 4; 5,6 = 6; 7,7' = 14;



1a 1b



6

Scheme 1.

8,9 = 8,10 = 7; OTigl: 3,4 = 7; 4,5 = 1.3].

Compound **4** (5 mg) was heated for 1 hr with 0.1 ml Ac_2O at 70°. After evaporation PTLC of the residue gave 3 mg **4a**, colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1760, 1740 (OAc), 1730 ($C{=}CCO_2R$), 1700 (C=O); MS *m/z* (rel. int.): 264.126 [M − HOAc, ketene]$^+$ (1) (calc. for $C_{15}H_{18}O_3$: 264.126), 246 [264 − H_2O]$^+$ (0.6), 164 [264 − RCO_2H]$^+$ (12), 83 [C_4H_7CO]$^+$ (100), 55 [83 − CO]$^+$ (62); ^{1}H NMR ($CDCl_3$): δ 5.82 (*d*, H-3), 2.46 (*ddd*, H-4), 5.65 (*dd*, H-5), 6.92 (*dt*, H-6), 4.81 and 4.73 (*br d*, H-7), 2.05 (*dqq*, H-8), 1.03 (*d*, H-9), 0.99 (*d*, H-10); OAc: 2.12 and 2.09 (*s*); OTigl: 6.97 (*qq*), 1.84 (*dq*), 1.90 (*br s*) [*J*(Hz): see compound **4**].

REFERENCES

1. Akhmedov, I. S., Kasymov, S. Z. and Sidyakin, G. P. (1970) *Khim. Prir. Soedin* **6**, 691.
2. Bohlmann, F., Jakupovic, J., Warning, U., Grenz, M., Chau-Thi, T. V., King, R. M. and Robinson, H. (1986) *Bull. Soc. Chim. Belg.* **95**, 707.
3. Sipma, G. and Van der Wal, B. (1968) *Rec. Trav. Chim. Pays-Bas* **87**, 715.
4. Appendino, G., Gariboldi, P., Nano, G. M. and Tetenyi, P. (1984) *Phytochemistry* **23**, 2545.
5. Khafagy, S. M., Al-Yahya, M. A., Ziesche, J. and Bohlmann, F., (1983) *Phytochemistry* **22**, 1821.
6. Chawla, A. and Dev, S. (1967) *Tetrahedron Letters* 4837.
7. Paton, W. F., Paul, I. C., Bajaj, A. G. and Dev, S. (1979) *Tetrahedron Letters* 4153.