

## 18-Hydroxyballonigrin, a New Diterpenoid from *Ballota acetobulosa*

By Giuseppe Savona and Franco Piozzi,\* Istituto di Chimica Organica, Università di Palermo, Via Archirafi, Palermo, Italy

James R. Hanson\* and Michael Siverns, School of Molecular Sciences, University of Sussex, Brighton, Sussex BN1 9QJ

The structure of 18-hydroxyballonigrin (1), isolated from *Ballota acetobulosa*, has been established by a combination of spectroscopic measurements and an inter-relationship with ballonigrin (3).

A NUMBER of furanoid diterpenoids of the labdane series have been isolated from *Ballota* (Labiatae) species. We have previously examined *B. nigra*<sup>1</sup> and *B. rupestris*.<sup>2</sup> In continuation of this work, we have studied a Greek species, *B. acetobulosa* and isolated a new diterpenoid, C<sub>20</sub>H<sub>24</sub>O<sub>5</sub>, (1). The i.r. and <sup>1</sup>H n.m.r. spectra showed that the oxygen functions were a primary alcohol, a  $\gamma$ -lactone, an  $\alpha\beta$ -unsaturated ketone and a  $\beta$ -substituted furan ring. In addition the <sup>1</sup>H n.m.r. spectrum (Table 1)

TABLE 1

<sup>1</sup>H N.m.r. signals (in CDCl<sub>3</sub>: p.p.m. from Me<sub>4</sub>Si)

Compound	20-H	18-H	17-H	5-H <sup>a</sup>	6-H <sup>a</sup>	14-H	15-H	16-H
(1)	1.08	3.73	1.80	2.56	4.95	6.28	7.23	7.34
(2)	1.10	4.14	1.83	2.41	4.80	6.28	7.23	7.35 <sup>b</sup>
(4)	1.10	3.56 <sup>c</sup>	1.82	2.60	4.75	6.28	7.23	7.35
(5)	1.08	3.95	1.82	2.60	4.73	6.28	7.25	7.30
(6)	1.08	3.20 <sup>d</sup>	1.83	2.48	4.64	6.28	7.25	7.35

<sup>a</sup> *J*<sub>5-6</sub> 6 Hz. <sup>b</sup> O-CO-CH<sub>3</sub> 2.08. <sup>c</sup> *J* 14 Hz. <sup>d</sup> *J* 12 Hz.

contained signals which were assigned to a tertiary methyl group and an olefinic methyl group. Spin decoupling experiments established that a doublet ( $\delta$  4.95,

TABLE 2

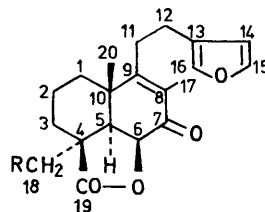
<sup>13</sup>C N.m.r. signals (in CDCl<sub>3</sub>: p.p.m. from Me<sub>4</sub>Si)

Carbon atom	Compound	
	(1)	(2)
1	30.2	30.2
2	17.7	17.5
3	22.5	23.1
4	48.8	46.6
5	45.6	45.7
6	77.3	76.7
7	193.5	192.6
8	131.2	131.4
9	166.6	166.2
10	36.4	36.3
11	29.4	29.4
12	24.2	24.2
13	123.8	123.7
14	110.6	110.6
15	143.2	143.2
16	138.8	138.9
17	29.0	28.8
18	67.5	67.5
19	180.1	177.6
20	12.1	12.1
O-CO-CH <sub>3</sub>		20.9 and 170.4

*J* 6 Hz) assigned to the proton attached to the  $\gamma$ -lactone ring, was coupled to a methine proton ( $\delta$  2.56) which

<sup>1</sup> G. Savona, F. Piozzi, J. R. Hanson, and M. Siverns, *J.C.S. Perkin I*, 1976, 1607; 1977, 497.

itself showed no further coupling. This data suggested that the compound was 18-hydroxyballonigrin (1). The alcohol readily gave a mono-acetate (2). The <sup>13</sup>C n.m.r. data of (1) and (2) (Table 2) were in accord with the relationship with ballonigrin and permitted the location of the primary alcohol at C-18. In particular when compared to ballonigrin<sup>1</sup> the C-4 singlet resonance had a downfield shift ( $\Delta\delta$  6.8) whilst both C-3 and C-5 showed an upfield  $\gamma$ -shift ( $\Delta\delta$  5.3 and 3.8 respectively). The chemical shift of the H-5 and H-6 resonances also displayed a downfield shift.



- (1) R = OH  
 (2) R = OAc  
 (3) R = H  
 (4) R = Cl  
 (5) R = OTs  
 (6) R = I

The relationship with ballonigrin was confirmed chemically. Treatment of 18-hydroxyballonigrin, under mild conditions with triphenylphosphine in carbon tetrachloride,<sup>3</sup> gave the 18-chloro-compound (4). However, reduction of this with tributyltin hydride afforded a complex mixture of products. 18-Hydroxyballonigrin formed an 18-monotoluene-*p*-sulphonate (5). Reduction of this with zinc and sodium iodide<sup>4</sup> gave ballonigrin (3) together with an 18-iodo-compound (6).

### EXPERIMENTAL

General experimental details have been described previously.<sup>1</sup> <sup>1</sup>H N.m.r. spectra were determined at 90 MHz on a Perkin-Elmer R 32 spectrometer.

*Extraction of Ballota acetobulosa.*—*B. acetobulosa* was collected on Mount Hymettus, Kaessariani, Athens, and identified in the Institute of General Botany, University of Athens. Air-dried leaves (0.5 kg) were powdered and extracted at room temperature with acetone (2 l) for 1 month. The extract was concentrated *in vacuo*, redissolved in ethyl acetate, washed with aqueous 10% sodium carbonate, dilute hydrochloric acid, and water, and then dried and evaporated. The crude residue (approx. 2 g) was chromatographed on a dry silica gel column (Merck, deactivated with 15% water). Elution with 30% ethyl

<sup>2</sup> G. Savona, F. Piozzi, J. R. Hanson, and M. Siverns, *J.C.S. Perkin I*, 1977, 322.

<sup>3</sup> J. B. Lee and I. M. Downie, *Tetrahedron*, 1967, **23**, 359.

<sup>4</sup> Y. Fujimoto and T. Tatsuno, *Tetrahedron Letters*, 1976, 3325.

acetate–light petroleum gave 18-hydroxyballonigrin (1) (500 mg), m.p. 171 °C,  $[\alpha]_D -2.4^\circ$  (*c* 0.2 in  $\text{CHCl}_3$ ) (Found: C, 70.1; H, 7.0.  $\text{C}_{20}\text{H}_{24}\text{O}_5$  requires C, 69.9; H, 6.9%),  $\nu_{\text{max}}$  3 480, 1 765, 1 655, 1 595, and 875  $\text{cm}^{-1}$ ;  $\lambda_{\text{max}}$  259 nm ( $\epsilon$  9 400); mass spec. *m/e* 344, 329, 316, 301, 203, 192, 175, 161, 105, 95, and 81 (base peak). The acetate (2), prepared with acetic anhydride in pyridine, was an oil (Found:  $M^+$  *m/e* 386.173.  $\text{C}_{22}\text{H}_{26}\text{O}_8$  requires 386.173), mass spec. *m/e* 386, 371, 343, 311, 298, 279, 231, 203 (base peak), 167, 161, 107, 105, 95, 82, and 81;  $\nu_{\text{max}}$  1 770, 1 745, 1 670, 1 595, and 875  $\text{cm}^{-1}$ .

*Reaction with Triphenylphosphine and Carbon Tetrachloride.*—18-Hydroxyballonigrin (30 mg) in carbon tetrachloride (20 ml) was heated under reflux with triphenylphosphine (50 mg) for 16 h. Chromatography on silica gave 18-chloroballonigrin (4) as needles, m.p. 125 °C (Found:  $M^+$  *m/e* 362.128.  $\text{C}_{20}\text{H}_{23}^{35}\text{ClO}_4$  requires 362.128), mass spec. *m/e* 362, 347, 319, 297, 203 (base peak), 191, 161, 105, 95, 82, and 81;  $\nu_{\text{max}}$  1 778, 1 666, 1 604, and 876  $\text{cm}^{-1}$ . Re-

action with tributyltin hydride in hexane gave a complex mixture of products (t.l.c.).

*Conversion into Ballonigrin (3).*—18-Hydroxyballonigrin (50 mg) in pyridine (2 ml) was treated with an excess of toluene-*p*-sulphonyl chloride overnight to afford the 18-mono-toluene-*p*-sulphonate (5) as an oil (Found:  $M^+$ , 498.170.  $\text{C}_{27}\text{H}_{30}\text{SO}_7$  requires *M*, 498.171), mass spec. 498, 483, 470, 455, 417, 326, 311, 298, 295, 270, 231, 217, 203, 189, 161, 95, and 81. The oil (40 mg) in dioxan (10 ml) was heated under reflux with sodium iodide (500 mg) and zinc dust (500 mg) for 72 h. Chromatography on silica afforded 18-iodoballonigrin (6) (8 mg) as an oil (Found:  $M^+$ , 454.064.  $\text{C}_{20}\text{H}_{23}\text{O}_4\text{I}$  requires *M*, 454.064) and ballonigrin (3) (10 mg) which was identified by its n.m.r. spectrum.

We thank Dr. S. Diamantoglou for the collection and identification of the plant material and NATO for a research grant.

[8/014 Received, 4th January, 1978]