Phytochemistry, Vol. 20, No. 8, pp. 2023–2024, 1981.
Printed in Great Britain.

0031–9422/81/082023–02 $02.00/0

OCCURRENCE OF MELITTOSIDE IN THE SEEDS OF *PLANTAGO MEDIA*

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(*Received* 22 *December* 1980)

Key Word Index—*Plantago media*; Plantaginaceae; ^{13}C NMR; 360 MHz ^{1}H NMR; iridoid diglycoside; melittoside.

Abstract—The ^{13}C NMR and 360 MHz ^{1}H NMR signals of melittoside and its acetate have been assigned.

INTRODUCTION

Melittoside (**1**) was isolated from *Melittis melissophyllum* (Labiatae) by Scarpati and Esposito in 1967 and was the first iridoid to be found to contain two molecules of sugar (glucose) [1]. It has so far been found in the families Scrophulariaceae and Labiatae [2]. In a chemotaxonomic survey of some *Plantago* species, a polar glycoside (substance C) was detected in the seeds and inflorescences of *Plantago media* L. [3]. After isolation we subsequently identified 'substance C' as melittoside on the basis of its UV, IR and ^{1}H NMR (100 MHz) spectra [1]. Thus, this is the first report of an iridoid diglycoside in the family Plantaginaceae. Due to the complexity of the ^{1}H NMR spectral pattern several signals in the original study were left unassigned. We have, therefore, carried out a detailed 360 MHz ^{1}H NMR analysis of **1** and its acetate (**1a**).

RESULTS AND DISCUSSION

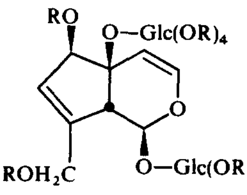
The 360 MHz ^{1}H NMR spectrum of melittoside (in D$_2$O) is very informative. Apart from the signal due to H-9 which is overlapping with the signals of the glucose protons, all the signals arising from the aglycone part are well resolved and the assignments are straight forward (see Experimental). The spin decoupling experiments, effected by irradiating the signals at δ 5.44 (H-1) which simplified the only signal at δ 3.35 into a singlet, established the assignment of H-9. The ^{1}H NMR of **1a** is similarly related. The assignments given are confirmed, where necessary, by double resonance experiments. Additionally, the ^{13}C NMR spectra of **1** and **1a** were studied. Compound **1** showed the expected signals for 21 carbons. The assignment of the signals was aided by the published data on monomelittoside (**2**) [4] and other related iridoid glucosides [5]. As a result of glucosylation at C-5, the α-carbon is shifted *ca* 7 ppm downfield, accompanied by significant upfield shifts of the signals of the β-carbons, C-4, C-6 and C-9, the effect being less noticeable at C-6. The present study further demonstrated that the anomeric carbon signal from the glucopyranosyl moiety of iridoid glucosides is deshielded in the decreasing order of primary (δ 102.0–103.3, linked at C-10/11) [6, 7], secondary (δ 99.0–100.5, linked at C-1) [5, 6] and tertiary (δ 98.2, linked at C-5) alcoholic β-D-glucopyranosides and finds precedence in other series [8].

EXPERIMENTAL

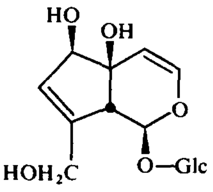
The general experimental procedures were as reported in a recent paper [4].

Plant material. Seeds of *Plantago media* L. were collected in Łódź, Poland. A voucher specimen of the plant material is deposited in the Herbarium of Instytut Badania Środowiska i Bioanalizy, Łódź, Poland.

Isolation of melittoside (**1**). Air-dried seeds (750 g) were cut into small pieces and continuously extracted in a Soxhlet with petrol (60–80°) and then with 85 % EtOH (3 × 1.2 l.). The EtOH extract was concd to *ca* 0.4 l. under red. pres. and kept in the refrigerator for 6 days when melittoside was separated (*ca* 0.08 %) as fine needles. This crystalline solid was passed through a column of Si



1 Melittoside: R = H
1a Melittoside decaacetate:
R = Ac; Glc = β-D-Glucose



2 Monomelittoside

gel (10 g Merck, 70–230 mesh) eluting with MeOH. The appropriate fractions were collected together and, after removal of the solvent, melittoside (*ca* 0.075 %) was crystallized from MeOH–EtOH (2:1).

Melittoside (**1**), mp 157–159°, $[\alpha]_D^{20}$ −41.9° ($c = 1.03$, MeOH); ^{1}H NMR (360 MHz, D_2O): δ 6.51 (1 H, *d*, $J = 6.5$ Hz, H-3), 5.86 (1 H, *dd*, $J = 1.8/2.0$ Hz, H-7), 5.44 (1 H, *d*, $J = 5.4$ Hz, H-1), 5.16 (1 H, *d*, $J = 6.5$ Hz, H-4), 4.58 (1 H, *s* (*br*), (H-6), 4.28/4.25 (2 H, AB-syst., $J = 15.2$ Hz, 2 H-10), 3.35 (1 H, *d*, $J = 5.4$ Hz, H-9); ^{13}C NMR (CD_3OD); aglycone: δ 94.18 (C-1), 143.42 (C-3), 105.26 (C-4), 80.06 (C-5), 79.92 (C-6), 128.21 (C-7), 147.34 (C-8), 50.55 (C-9), 60.94 (C-10); glucose: δ 99.69 (C-1′), 98.15 (C-1″), 74.90/75.11 (C-2′/2″), 78.22/78.43 (C-3′/3″ or C-5′/5″), 70.83/71.67 (C-4′/4″), 77.19/78.11 (C-5′/5″ or C-3′/3″), 62.12/62.74 (C-6′/6″).

Melittoside decaacetate (**1a**) was obtained (pyridine and Ac_2O) as an amorphous powder. $[\alpha]_D^{20}$ −43.4° ($c = 1.1$, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$): δ 6.37 (1 H, *d*, $J = 6.7$ Hz, H-3), 5.77 (1 H, *dd*, $J = 1.8/2$ Hz, H-7), 5.38 (1 H, *dd*, $J = 2/2$ Hz, H-6), 5.28 (1 H, *d*, $J = 1.6$ Hz, H-1), 5.27 (1 H, *d*, $J = 6.7$ Hz, H-4), 4.70 (2 H, *s* (*br*), 2 H-10), 3.82 (1 H, *s* (*br*), H-9), 4.74 (1 H, *d*, $J = 8.2$ Hz, H-1′), 4.87 (1 H, *d*, $J = 8.6$ Hz, H-1″), 3.71–3.78 and 3.90–3.97 (2 H, *m*, H-5′/5″), 4.09–4.17 and 4.22–4.34 (4 H, *m*, 2 H-6′/6″), 4.70–5.50 (H-2′/3′/4′/5′ and H-2″/3″/4″/5″), 1.94–2.19 (10 × OCOMe); ^{13}C NMR ($CDCl_3$); aglycone: δ 93.99 (C-1), 142.63 (C-3), 109.90 (C-4), 77.01 (C-5), 82.83 (C-6), 127.18 (C-7), 141.06 (C-8), 54.91 (C-9), 60.92 (C-10); glucose: 96.92 (C-1′), 95.80 (C-1″), 70.50/71.08 (C-2′/2″), 72.70/72.49 (C-3′/3″ or C-5′/5″), 68.10/68.47 (C-4′/4″), 72.35/71.37 (C-5′/5″ or C-3′/3″), 61.52 (62.06 (C-6′/6″), 169.47–170.72 ($\underline{C}$OMe), 20.54–20.71 ($CO\underline{C}H_3$).

Acknowledgements—We thank Prof. C. Trogolo, Istituto di Chimica Organica, Università di Roma, for an authentic sample of melittoside decaacetate, and the Wilhelm Doerenkamp Foundation for financial support.

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Phytochemistry, Vol. 20, No. 8, pp. 2024–2026, 1981.
Printed in Great Britain.

0031-9422/81/082024-03 $02.00/0

NOTONIPETRONE-LIKE SESQUITERPENES FROM *SENECIO KLEINIA**

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(*Received* 2 *December* 1980)

Key Word Index—*Senecio kleinia*; Compositae; sesquiterpenes; notonipetrone derivatives.

Abstract—Five new notonipetrone-like sesquiterpenes have been isolated from the roots of *Senecio kleinia* and their structures elucidated.

Only pyrrolizidin alkaloids [1] and quercetin [2] have been isolated from *Senecio kleinia* Less., a plant which is widespread on the Canary Islands. A re-investigation of the aerial parts showed that in addition to caryophyllene and γ-humulene, large amounts of **7** [3] and **8** [4] were present. The roots contained a complex mixture of sesquiterpene esters, which could be separated only with difficulty. Finally six compounds were obtained, but only one of them, the ketone notonipetrone (**1**) [4], has been isolated previously. The structures **2**–**6** of the other sesquiterpenes followed from the ^{1}H NMR data (Table 1), which were in part similar to those of **1**. The ^{1}H NMR spectrum of **2** obviously only differed in the signals of the ester residue at C-7. The signals of the isovalerate were replaced by the typical signals of a 4-methyl senecioate. Compound **3**, however, was a ketone with a free hydroxyl and two ester groups, a 2-methylbutyrate and a 4-methylsenecioate. The ^{1}H NMR data clearly showed that

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*Part 351 in the series "Naturally Occurring Terpene Derivatives". For Part 350 see Bohlmann, F., Zdero, C., Jakupovic, J., Robinson, H. and King, R. M. (1981) *Phytochemistry* **20** (in press).