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A NEW SESQUITERPENE LACTONE FROM *ELEPHANTOPUS SCABER*

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Key Word Index—*Elephantopus scaber*; Compositae; lupeol; stigmasterol; 11,13-dihydrodeoxyelephantopin.

Abstract—A methanolic extract of the plant *Elephantopus scaber* was found to contain lupeol, stigmasterol and a new germacranolide dilactone 11,13-dihydrodeoxyelephantopin.

INTRODUCTION

The synthesis of variants of known cancer chemotherapeutic agents has resulted in the production of several hundred compounds but with little improvement in activity over the prototype drugs. Thus there exists a great demand for new templates for the synthetic chemist to use in designing superior chemotherapeutic agents. In keeping with this need, recent work in the isolation and characterization of tumor inhibitors has resulted in a series of new growth inhibitory compounds [1] including some sesquiterpenoid lactones. Recent work has revealed the importance of the α-methylene lactone function for the biological activity of these compounds [1]. Two novel sesquiterpenes with marked anti-tumor activity have been isolated from *Elephantopus elatus* [2].

The National Institute of Cancer has established that methanolic extracts of *E. scaber* also exhibit anti-tumor activity [3]. Therefore we undertook a programme to isolate and characterize the compounds responsible for the biological activity and in this paper we report the isolation and characterization of a new sesquiterpenoid lactone (1) from such an extract. The compound has been described [4] previously as a reduction product of deoxyelephantopin isolated from Taiwanese *E. scaber* but this is its first description as a natural product.

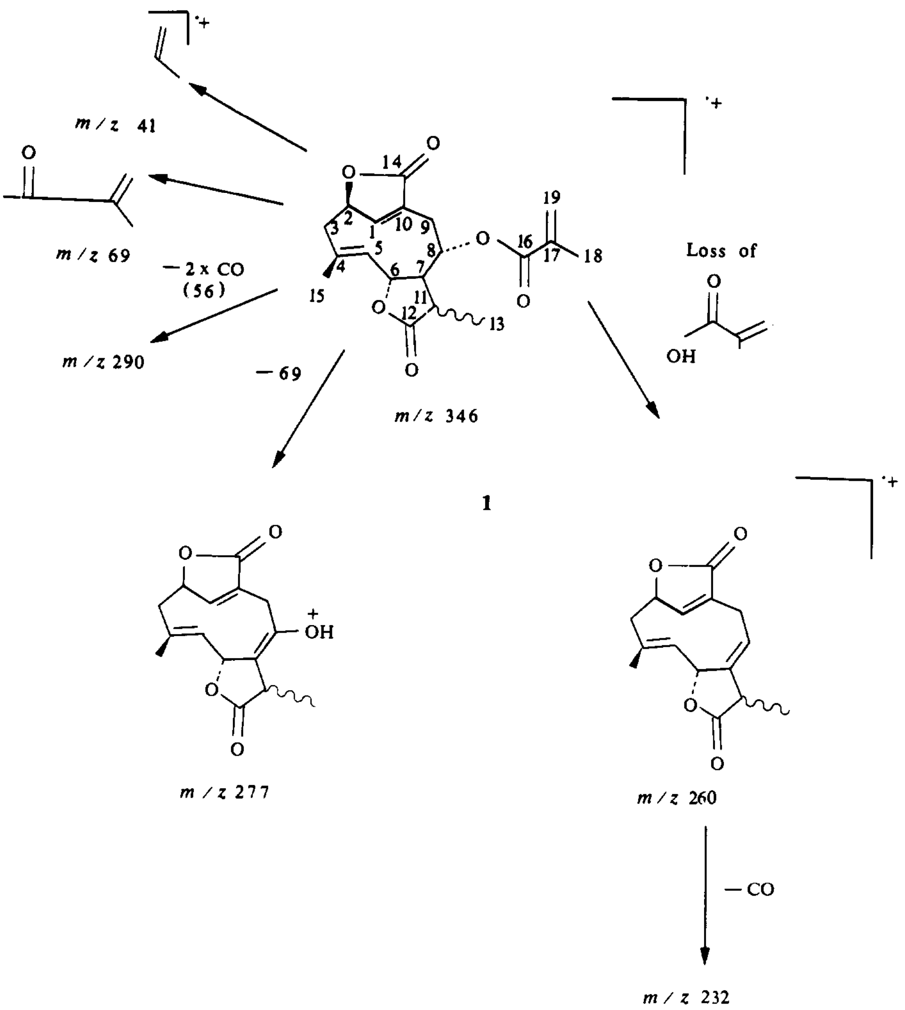
RESULTS AND DISCUSSION

Powdered air-dried plant material was extracted with hot methanol and the resulting extract partitioned between 10% aqueous methanol and petrol. The aqueous methanol extract was evaporated to dryness and the residue chromatographed on a Si gel column. The first two compounds to be eluted from the column were lupeol and stigmasterol and were identified by comparison of their physical data (UV, IR, ^{1}H NMR) with those of authentic samples. In subsequent fractions 11,13-dihydrodeoxyelephantopin (**1**) mp 234° was eluted. High resolution mass spectrometry indicated that **1** has the molecular formula $C_{19}H_{22}O_6$. Its IR spectrum showed bands at 1700 cm^{-1} and 1260 cm^{-1} suggesting the presence of an α,β-unsaturated ester. That this was a methyl-acrylate ester was suggested by the peak at m/z 260 $[M - C_4H_6O_2]^+$ in its mass spectrum. The IR carbonyl absorption at 1740 cm^{-1} together with a ^{1}H NMR signal at δ 6.84 due to a vinyl proton β to a carbonyl, indicated the presence of an α,β-unsaturated γ-lactone grouping. The presence of an IR absorption band at 1765 cm^{-1} suggested the presence of a saturated γ-lactone grouping. This was supported by a doublet at δ 1.24 (3H, H-13) and a multiplet at 2.7 (1H, H-11) in the ^{1}H NMR spectrum. The physical data of **1**, particularly the ^{1}H NMR and mass spectra (Scheme 1) suggested that the compound was a sesquiterpenoid dilactone (Table 1). A detailed examination of the ^{1}H NMR and mass spectra of **1** showed that they

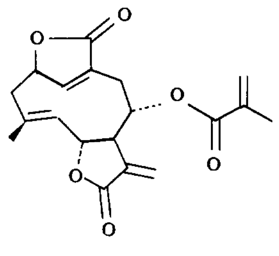
Table 1. ^{1}H NMR spectrum of 11,13-dihydrodeoxyelephantopin*

δ (ppm)	Multiplicity (J in Hz)	No. of protons	Assignment
6.84	*s*	1	H-1
6.16	*d* (1)	1	H-19
5.68	*d* (1)	1	H-19
5.5–5.4	*m*	2	H-2, H-6
4.9	*d* (12)	1	H-5
4.52	*m*	1	H-8
2.5–3.2	*m*	6	H-3, H-7, H-9
1.96	*d* (1)	3	H-18
1.85	*d* (1)	3	H-15
1.24	*d* (8)	3	H-13

*The spectrum was recorded at 90 MHz in $CDCl_3$.



Scheme 1.



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are very similar to those of deoxyelephantopin (**2**) [4, 5] but closer to those of dihydrodeoxyelephantopin, a chemical reduction product of **2** [4]. Hence the structure of the sesquiterpenoid dilactone may be formulated as **1**.

EXPERIMENTAL

E. scaber was collected during Feb. 1980 at Kandy, Sri Lanka. Identity of compounds was established by mp, mmp, TLC and IR. ^1H NMR spectra were recorded at 90 MHz and are given in δ (Hz) relative to TMS; Mps were determined in open capillaries and are uncorr.

Isolation. The dried powdered plant of *E. scaber* (600 g) was extracted with hot MeOH for 3 days. Evaporation of the solvent gave a dark brownish-green syrup (7.2 g) which was partitioned between petrol (62–82°) and 10% aq. MeOH. The aq. MeOH layer was evaporated and the dark brownish-green solid (4 g) obtained was chromatographed on Si gel (200 g). Fractions from the column were monitored by TLC

(Si gel, $CHCl_3$). The fraction eluted with petrol–C_6H_6 (9:1) gave lupeol (720 mg), mp 215°. The next fractions eluted with the same eluent gave stigmasterol (330 mg), mp 168°. Elution with petrol–C_6H_6 (3:1) gave 11,13-dihydrodeoxyelephantopin (**1**). This was purified by prep. TLC (Si gel, $CHCl_3$) and on crystallization from $CHCl_3$–petrol (1:1) gave white needles (12 mg), mp 234°. MS m/z (rel. int.): 346 (1.62), 290 (1.15), 277 (0.84), 260 (22.15), 232 (8.94), 214 (24.62), 203 (11.86), 188 (9.71), 175 (11.62), 147 (9.96), 121 (14.40), 91 (20.13), 83 (49.48), 69 (100), 55 (40), 41 (100). Accurate mass of peak m/z 260 ($C_{15}H_{16}O_4$): 260.1037 $C_{15}H_{16}O_4$ requires 260.1047. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3020, 1765, 1740, 1700, 1630, 1260. UV λ_{max}^{MeOH} 217 nm ($\epsilon = 15{,}500$). ^{1}H NMR (90 MHz, $CDCl_3$): δ 1.24 (3H, *d*, $J = 8$ Hz, H-13), 1.85 (3H, *d*, $J = 1$ Hz, H-15), 1.96 (3H, *d*, $J = 1$ Hz, H-18), 2.5–3.2 (6H, *m*, H-3, H-7, H-9), 4.52 (1H, *m*, H-8), 4.9 (1H, *d*, $J = 12$ Hz, H-15), 5.4–5.5 (2H, *m*, H-2, H-6), 5.68 (1H, *d*, $J = 1$ Hz, H-19), 6.16 (1H, *d*, $J = 1$ Hz, H-19), 6.84 (1H, *s*, H-1).

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ENT-BEYER-15-ENE DERIVATIVES FROM *NIDORELLA ANOMALA**

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Key Word Index—*Nidorella anomala*; Compositae; Astereae; diterpenes; *ent*-beyerene derivatives.

Abstract—*Nidorella anomala* afforded in addition to known beyerene derivatives three new ones.

Six species from the South African genus *Nidorella* (Compositae, tribe Astereae) have been investigated chemically. These species all contain dehydrofalcarinone or its derivatives [1, 2], while only three species afforded diterpenes, most of them being *ent*-clerodanes [1, 2]. Two species contained *seco*-clerodane or *seco*-labdane derivatives [1, 2]; two sesquilimonene derivatives [1, 2] and coumarins such as obliquin were isolated from two species [1, 2]. We have now investigated *Nidorella anomala* Steetz, which differs from all the other species by its 3–4-lobed, non-radiate outer flowers, with sparse pappus shorter than the tube [3]. The roots afforded the dehydrofalcarinone derivative **10** [1], while the aerial parts gave coumarin, obliquin (**11**) [4] and the *ent*-beyer-15-ene derivatives **1** [5], **3** [6] and **4** [7] as well as three further ones, the hydroxy acid **5**, the malonate **7** and the diester **9**. The structure of **5**, which was transferred to its methyl ester, followed from the ^{1}H NMR spectrum (Table 1). Most signals were close to those of **2**, only the additional downfield signals at δ 3.07 and 3.32 indicated the presence of a hydroxyl group. The former signal was a three-fold doublet and coupled with the broadened doublet at δ 3.32. The couplings observed showed that an equatorial hydroxyl group was present, which obviously was hydrogen bonded with the carbomethoxy group as followed from the IR spectrum, the large coupling observed in the ^{1}H NMR spectrum and the downfield shift signal of H-18 if compared with the chemical shift of this signal in the spectrum of **2**. The second diterpene was transformed to the methyl ester **8**. The structure followed from the mass spectrum and the ^{1}H NMR spectral data (Table 1). In addition to the molecular formula ($C_{24}H_{36}O_4$), the elimination of $O{=}C{=}CHCO_2Me$, HO_2CCH_2Me and $CH_2OCOCH_2CO_2Me$ supported the presence of the malonate residue. The ^{1}H NMR spectrum showed the typical doublets of H-19 and a two-proton singlet at δ 3.38, typical of a malonate, while the chemical

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*Part 410 in the series "Naturally Occurring Terpene Derivatives". For Part 409 see Bohlmann, F., Zdero, C., Robinson, H. and King, R. M. (1982) *Phytochemistry* **21** (in press).