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NEW DIESTERS OF 12-DEOXY-PHORBOL

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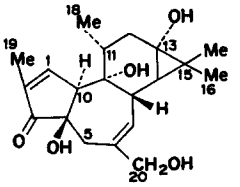
Key Word Index—*Euphorbia* species; Euphorbiaceae; 12-deoxyphorbol esters; diterpene.

12-Deoxy-phorbol esters are potent toxins which produce severe inflammation of the skin [1]. They are therefore of interest in the study of the complex biochemical sequences involved in the inflammatory process in mammals [2]. Their occurrence in *Euphorbia* species is of particular interest in this respect due to a recent failure to synthesize the 12-deoxy-phorbol series of irritants from the phorbol series [3]. We wish to report the isolation of three new irritant diesters of 12-deoxy-4βOH-phorbol which occurred as only minor components of a complex mixture of known esters [2,4] from the latex of *Euphorbia* species.

Plant material. E. coerulescens; *E. fortissima*; *E. polyacantha.*

Present work. Approximately 10 ml fresh latex was used for the isolations. The irritants were extracted and purified by a combination of solvent partition, column chromatography and TLC as previously described [4]. Final purification was by preparative TLC on Si gel (500 μm layers activated at 120° for 1 hr after buffering at pH 7·0) developing with $CHCl_3$–C_6H_6–Et_2O (1:3:3) as solvent. Clear glassy resins were produced which failed to crystallize from several solvents, but which were homogeneous by TLC [5] and MS.



(1)

The resins had similar IR spectra (ν_{max}, 3385, 1725, 1705, 1695 and 1630 cm^{-1}. solvent $CHCl_3$) and CD spectra (negative cotton effects at 272 and 360 nm, solvent MeOH). Hydrolysis [$Ba(OH)_2$ in MeOH under N_2] afforded a common parent alcohol (**1**) in *ca* 40% yield. This alcohol was unstable and was converted to its diacetate [6] before recrystallising from Me_2CO (mp 138°). The NMR spectrum (60 MHz, $CDCl_3$; TMS = 0·00 ppm) exhibited signals at δ 0·89 *d* (*J* 4 Hz, 3H-18, H-14); δ 1·16 *d* (*J* 8 Hz, 6H-16, 17); δ 1·80 *d* (*J* 2·1 Hz, 3H-19); δ 2·05 (6H–Me–CO–); δ 2·18 *s* (2H-12); δ 2·44 *s* (2H-5); δ 3·02 *m* (H-8); δ 3·29 *m*(H-10); δ 4·47 *s* (2H-20); δ 5·75 *d* (*J* 4·3 Hz, H-7); δ 7·64 *s* (H-1); δ 2·47 and δ 5·58 (2-OH-deuterium exchange). The MS exhibited a molecular ion at *m/e* 432 ($M^+C_{24}H_{32}O_7$) with significant fragment ions at *m/e* 414 (M-18); 372 (M-60); 354 (M-60 + 18); 336 (M-36 + 60); 312 (M-120); 294 (M-120 + 18) in the upper region of the spectrum. The TLC [5] and GLC [6] data were identical to 12-deoxy-4βOH-phorbol-13,20-diacetate.

Ester A: 12-*deoxy*-4βOH-*phorbol*-13-*dodecanoate*-20-*acetate.* This resin (10 mg) was isolated from latex of *E. coerulescens.* It had an R_f value of 0·8 in the system above, and produced an orange fluorescence under UV light after spraying with 60% H_2SO_4 and heating. Most of the signals in the NMR spectrum could be characterized as arising from the parent alcohol [7]. In addition, it had 3H signal at δ 0·89 and an 18H, *s* at δ 1·27, a 2H triplet at δ 2·32 and one acetate at δ 2·05. The MS *m/e* 572 (M^+ $C_{34}H_{52}O_2$) and prominent fragment ions at *m/e* 512 (M-60); 372 (M-200); 312 (M-60 + 200); 294 (M-60 + 200 + 18). Transesterification in 0·5 M KOH in MeOH at room temp. produced a low R_f value monoester. [M^+ $C_{32}H_{50}O_6$ at *m/e* 530, fragment ions by MS at *m/e* 512 (M-18); 494 (M-36); 330 (M-

200); 312 (M-200 + 18).] Acetylation of the mono-ester produced a compound identical by TLC and MS to *ester A*. Hydrolysis in $Ba(OH)_2$ followed by methylation and GLC[8] confirmed the presence of dodecanoic acid.

Ester B: 12-*deoxy*-4β*OH*-*phorbol*-13-*dodecenoate*-20-*acetate*. Resin B (5 mg: R_f value 0·75, orange by UV as before) was isolated from *E. fortissima* latex. The NMR spectrum as before suggested the presence of acetic and dodecenoic acids as esterifying moieties at C-20 and C-13 of (**1**). In the MS the resin had an M^+ ion at *m/e* 570 (M^+ $C_{34}H_{50}O_7$) and fragment ions at *m/e* 510 (M-60); 494 (M-60 + 18); 372 (M-198); 312 (M-198 + 60); 294 (M-198 + 60 + 18). Transesterification produced a mono-ester [M^+ $C_{32}H_{48}O_6$, at *m/e* 528 and fragment ions by MS at *m/e* 510 (M-18); 492 (M-36); 330 (M-198); 312 (M-198 + 18]. Acetylation of the mono-ester produced *ester B*. After complete hydrolysis dodecenoic acid was identified by GLC as before.

Ester C: 12-*deoxy*-4β*OH*-*phorbol*-13-*octenoate*-20-*acetate*. This ester (1·5 mg) was isolated from *E. polyacantha* (R_f value 0·72, orange by UV as before). It exhibited a molecular ion in the MS at *m/e* 514 (M^+ $C_{30}H_{42}O_7$) and fragment ions at *m/e* 372 (M-142); *m/e* 454 (M-60); *m/e* 312 (M-60 + 142); *m/e* 294 (M-60 + 142 + 18). Transesterification produced a mono-ester. (MS exhibited M^+ at *m/e* 472, $C_{28}H_{40}O_6$, and fragment ions at *m/e* 454 (M-18); 436 (M-36); 330 (M-142). Octenoic acid was identified by GLC after hydrolysis. Acetylation of the mono-ester produced *ester C*.

For *esters B* and *C* no attempt was made to assign the position of the double bond in the side chain. From a chemotaxonomic point of view it was of interest to note that these three succulent *Euphorbia* species, which are indigenous to Africa, all contained esters of the same parent alcohol (**1**).

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DITERPENES FROM THREE *SIDERITIS* SPECIES*

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Plants. Sideritis chamaedryfolia Cav., *Sideritis hyssopifolia* L. and *Sideritis luteola* Font Quer. *Sources.* Near Villena (Alicante), Puerto de Pajares (León) and Sierra de Filabres (Almeria),

* Part 24 in the series *Constituents of* Sideritis. For part 23 see Von Carstenn-Lichterfelde, C., Panizo, F. M., Quesada, T. G., Rodriguez, B., Valverde, S., Ayer, W. A. and Ball, J-A. H. *Can. J. Chem.* (in press).