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A NEW INGENOL TYPE DITERPENE FROM THE IRRITANT FRACTIONS OF *EUPHORBIA MYRSINITES* AND *EUPHORBIA BIGLANDULOSA*

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Key Word Index—*Euphorbia myrsinites*; *E. biglandulosa*; Euphorbiaceae; 5-deoxyingenol; ingenol; diterpenes.

The absolute configuration of ingenol the parent alcohol of several irritant and co-carcinogenic esters from *Euphorbia ingens* and *E. lathyris* has been established by X-ray crystallography.[1] Recently this diterpene has been reported from several other *Euphorbia* species.[2,3] We have examined the latices of *E. myrsinites* and *E. biglandulosa* and found them to contain ingenol, isolated as the triacetate 1, together with a minor component which we have assigned as 5-deoxyingenol diacetate 2 by comparison of spectral data.

Present work. The biologically active dried latex (1·5 g) yielded 500 mg of acetone soluble extract. After partition with hexane, followed by hydrolysis, 150 mg of resin was obtained, consisting of ingenol ($M^+ C_{20}H_{28}O_5$) and a minor component ($M^+ C_{20}H_{28}O_4$). Acetylation and preparative TLC on silica gel produced two residues, recrystallised from MeOH. The low R_f value compound m.p. 195–7°, $M^+ C_{26}H_{34}O_8$ yield 10 mg, was pure by TLC in several systems[4] and by GLC[3] where it co-chromatographed with authentic ingenol triacetate (**1**). IR ($CHCl_3$ KBr microcells) 3430, 1740, 1705, 1640 cm^{-1}; NMR $CDCl_3$ (tetramethylsilane $\delta = 0{\cdot}00$ ppm), 6·28 (H-7*d*), 6·09 (H-1*s*), 5·36 (H-5*s*), 4·93 (H-3*s*), 4·51, 4·08 (H_2-20, *JA*/B = 11·0 cps), 4·27 (H-8*d*, *J* H-7/H-8 5·5 cps), 3·22 (1OH deuterium exchange); 2·21, 2·12, 2·0 (3 MeCO); 1·78 (H_3-19*d*), 1·05–1·10 (3 Me); 0·92 (H-14) ppm. C.D. solvent methanol 202 [θ] = +21 780; 210 nm [θ] = +5148; 224 nm [θ] = −20064; 300 nm [θ] = +3003. The high R_f value compound mp 205–7°, $M^+ C_{24}H_{32}O_6$ yield 6 mg, was considered by TLC migrations and colour reactions[4] to be an ingenol derivative, in agreement also with the short retention time by GLC.[3] IR ($CHCl_3$ KBr microcells) 3430, 1740, 1705, 1640 cm^{-1}. NMR $CDCl_3$ (tetramethylsilane $\delta = 0{\cdot}00$ ppm) 6·09 (H-1); 5·82 (H-7*d*); 4·93 (H-3*s*); 4·04, 3·95 (H_2-20) *JA*/B = 2·75 cps); 4·30 (H-8*d*), 3·21 (1-OH deuterium exchange); 2·24, 2·11 (2MeCO), 1·74 (H_3-19*d*); 1·05–1·10 (3Me), 0·92 (H-14) ppm. C.D. solvent methanol [θ] 204 nm = +9541, 221 nm = −8154, 302 nm = +1090.

The high resolution MS (4 ppm) indicated identical ions in the low mass range for the acetates of (**1**) and (**2**). *m/e* 81 (34%) C_6H_9; *m/e* 93 (27%) C_7H_9; *m/e* 121 (76%) C_8H_9O; *m/e* 135 (37%) $C_9H_{11}O$; *m/e* 151 (22%) $C_9H_{11}O_2$; *m/e* 163 (16%) $C_{11}H_{15}O$; *m/e* 175 (18%)

[1] ZECHMEISTER, K., BRANDL, F., HOPPE, W., OPFERKUCH, H. J. and ADOLF, W. (1970) *Tetrahedron Letters*, **47**, 4075; HECKER, E. (1971) *Pharmacognosy and Phytochemistry*, 1st *Int. Cong.* (H. WAGNER and L. HÖRHAMMER ed.), pp. 147–165. Springer, New York.

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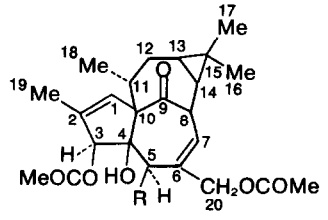
[3] EVANS, F. J. and KINGHORN, A. D. (1974) *Phytochemistry*, **13**, 1011.

[4] EVANS, F. J. and KINGHORN, A. D. (1973) *J. Chromatog.*, **87**, 443.

$C_{11}H_{11}O_2$. Similarity was also evident in the higher mass range, compound (**1**), *m/e* 251 (21%) 1 part $C_{18}H_{19}O$, 1 part $C_{17}H_{15}O_2$; *m/e* 294 (30%) $C_{20}H_{22}O_2$; *m/e* 312 (32%) $C_{20}H_{24}O_3$; *m/e* 354 (12%) $C_{22}H_{26}O_4$; *m/e* 414 $C_{24}H_{30}O_6$ (20%); compound (**2**) *m/e* 253 (20%) 1 part $C_{18}H_{21}O$, 1 part $C_{17}H_{17}O_2$; *m/e* 296 (30%) $C_{20}H_{24}O_2$; *m/e* 314 (23%) $C_{20}H_{26}O_3$; *m/e* 356 (13·5%) $C_{22}H_{28}O_4$.



(1) Ingenol triacetate, R = OCOMe
(2) 5-Deoxyingenol diacetate, R = H

Methanolysis of (**2**) produced a monoacetate ($M^+C_{22}H_{30}O_5$) which in the mass spectrum lost 42 units from the molecular ion indicating a primary acetate. Treatment of (**1**) and (**2**) with acid produced spots of lower R_f values. In the NMR of these compounds most of the signals were characterized from the spectra of the parent acetates but only one methyl group was evident at δ 1·05 (H_3-18*d*), and there was a paramagnetic shift of the C-17 and C-16 methyl groups to δ 1·24 and δ 1·55, signals at δ 5·6 (H-13) and δ 4·68 (H-15) and the absence of δ 0·92 (H-14) suggested the opening of ring D with the localization of the double bond at C13–14.

On the basis of TLC and colour reactions, GLC, mass spectra and NMR compound (**2**) is a deoxyingenol. Its configuration about the $\beta\gamma$-keto of ring B and C is the same as ingenol triacetate by circular dichroism spectra. The persistence of the signal at δ 4·93 in the NMR spectrum suggests the presence of a secondary acetate at C-3, and the primary acetate at C_{20} is evident from the NMR signals at δ 4·51 and δ 4·08, and further by loss of 42 mass units from the molecular ion of the monoacetate. Compound (**2**) is therefore assigned as 5-deoxyingenol isolated as the diacetate and it possibly exists in the plant as the ester of the 3 and 20 hydroxyl groups.

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