Phytochemistry, 1973, Vol. 12, pp. 703 to 705. Pergamon Press. Printed in England.

NEW SESQUITERPENOID ALKALOIDS FROM *EUONYMUS EUROPEA*

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(*Received* 13 *September* 1972. *Accepted* 3 *October* 1972)

Key Word Index—*Euonymus europea*; Celastraceae; 2,5-bisdeacetylevonine; 2-deacetylevonine; evonine; NMR; selective deacylation–bromobenzylation.

Abstract—Two new minor alkaloids from seeds of *Euonymus europea* L. have been characterised as 2-deacetylevonine and 2,5-bisdeacetylevonine by NMR. A selective one-step 5-deacetylation-bromobenzylation reaction of evonine is reported.

INTRODUCTION

Various sesquiterpene alkaloids characterize certain members of the Celastraceae. The structure of a key representative, maytoline (*Maytenus ovatus* Loes.) has been established by X-ray analysis.[1] From this, with further chemical investigation, the constitution of evonine (I),[2] the major base of *Euonymus europea* L.[3] and *E. sieboldiana* Blume, has been determined. A number of minor alkaloids in *Euonymus* sp. have now been recognised[4] and the structure of one, neoevonine, has recently been confirmed by X-ray methods.[5]

RESULTS

The basic fraction of an ether extract of ground seeds of *E. europaea* was chromatographed on neutral alumina. The fraction eluted by chloroform was separated by preparative TLC into five compounds. Three were recognized, by comparison of their physical and spectroscopic data with the literature values, as evonine,[2] neo-evonine,[4a] and evonoline.[4d] The other two were new alkaloids, $C_{34}H_{41}NO_{16}$ and $C_{32}H_{39}NO_{15}$. Comparison of their spectra with those of evonine indicated them to be 2-deacetylevonine (II) and 2,5-bisdeacetylevonine (III).

UV and IR data were similar to those of evonine (see Experimental); the NMR data were definitive and are correlated in Table 1. 2-Deacetylevonine shows one acetyl methyl less, and one hydroxyl group more, than evonine, in agreement with the molecular formula, and the 2-H is upfield (1·29 ppm) from its position in evonine (absence of a 2-ester function). 2,5-Bisdeacetylevonine shows only three acetyl methyls in its NMR (obtained by spectrum

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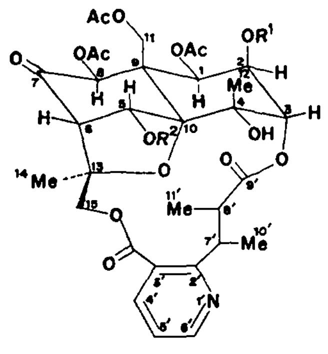

(I) $R^1 = R^2 = Ac$
(II) $R^1 = H$; $R^2 = Ac$
(III) $R^1 = R^2 = H$
(IV) $R^1 = Ac$; $R^2 = p\text{-}BrC_6H_4CH_2$
(V) $R^1 = Ac$; $R^2 = p\text{-}IC_6H_4CH_2$

accumulation), and both 2-H and 5-H are at higher field than the corresponding evonine signals (1·34 and 1·16 ppm respectively).

TABLE 1. NMR DATA ($CDCl_3$) FOR *E. europea* ALKALOIDS

Evonine	(1)	1·32 (*dd*, *J* 5, 2 Hz, 6′-H); 3·28 (*d*, *J* 1 Hz, 5-H); 4·43 (*s*, 8-H); 5·42 (*d*, *J* 13 Hz, 11-H); 5·33 (*m*, 7′-H); 8·39 (*s*, 14-H); 7·77, 7·85, 7·90, 7·95, 8·11 (5 × MeCO);	1·93 (*dd*, *J* 8, 2 Hz, 4′-H); 3·96 (*d*, *J* 12 Hz, 15-H); 5·22 (*d*, *J* 3 Hz, 3-H); 4·71 (*t*, *J* 3 Hz, 2-H); 7·41 (*m*, 8′-H); 8·39 (*s*, 12-H);	2·74 (*dd*, 5′-H); 4·29 (*d*, *J* 3 Hz, 1-H); 5·18 (*d*, *J* 13 Hz, 11-H); 6·24 (*d*, *J* 12 Hz, 15-H); 8·57 (*d*, *J* 7 Hz, 10′-H); 8·78 (*d*, *J* 7 Hz, 11′-H); *5·33 (OH)
2-Deacetyl-evonine	(2)	1·22 (*m*, 6′-H); 3·22 (*bs*, 5-H); 4·37 (*s*, 8-H); 6·15 (*m*, 7′-H); 5·40 (*d*, *J* 13 Hz, 11-H); 8·46 (*s*, 14-H); 7·84, 7·90, 8·02, 8·02 (4 × MeCO);	1·67 (*dd*, *J* 3, 7 Hz, 4′-H); 4·18 (*d*, *J* 12 Hz, 15-H); 4·86 (*d*, *J* 3 Hz, 3-H); 7·35 (*m*, 8′-H); 6·00 (*t*, *J* 3 Hz, 2-H); 8·76 (*s*, 12-H);	2·67 (*dd*, 5′ H); 4·27 (*d*, *J* 3 Hz, 1-H); 4·97 (*d*, *J* 13 Hz, 11-H); 8·40 (*d*, *J* 8 Hz, 10′-H); 6·13 (*d*, *J* 12 Hz, 15-H); 8·84 (*d*, *J* 7 Hz, 11′-H); *5·08, 5·33 (2 × OH)
2,5-Bisdeacetylevonine	(3)	1·23 (*m*, 6′-H); 4·64 (*d*, *J* 1 Hz, 5-H); 4·41 (*s*, 8-H); 5·50 (*d*, *J* 13 Hz, 11-H); 5·72 (*m*, 7′-H); 8·39 (*s*, 14-H); 7·87, 7·98, 8·03 (3 × MeCO);	1·66 (*bd*, 4′-H); 3·96 (*d*, *J* 13 Hz, 15-H); 4·76 (*d*, *J* 3 Hz, 3-H); 6·05 (*t*, *J* 3 Hz, 2-H); 7·36 (*m*, 8′-H); 8·72 (*s*, 12-H);	2·79 (*dd*, 5′H); 4·33 (*d*, *J* 3 Hz, 1-H); 4·82 (*d*, *J* 13 Hz, 11-H); 6·26 (*d*, *J* 13 Hz, 15-H); 8·43 (*d*, *J* 7 Hz, 10′-H); 8·79 (*d*, *J* 7 Hz, 11′-H); *3·61, 3·77 (2 × OH)

For heavy atom introduction, via *p*-bromo- and *p*-iodobenzyl ethers for X-ray purposes, evonine, with its one primary and five secondary hydroxyls already acylated, and only a hindered tertiary hydroxy remaining, appeared an unresponsive molecule. Stirring at room temperature in dimethylformamide containing silver oxide and *p*-halogeno-benzyl bromide was found, however, to selectively deacetylate C-5 and bring about benzylation in the same position. In this way (IV), $C_{41}H_{46}NO_{16}Br$, and (V), $C_{41}H_{46}NO_{16}I$ were obtained. In both cases crystals contained two molecules in the asymmetric unit and although the halogen could be located by Patterson synthesis the contribution to the phases by the heavy atom was insufficient to reveal any recognisable light atoms in subsequent Fourier summations.

EXPERIMENTAL

Extraction of seeds of Euonymus europaea. Ground seeds (45 kg) were percolated with light petrol. (b.p. 40–60°) and then extracted with the same solvent for 2 weeks in a Soxhlet. Extraction was continued with Et_2O. The concentrated Et_2O extract was washed with dil. HCl, and the acid washing neutralized and extracted with $CHCl_3$. The combined $CHCl_3$ extracts were washed with H_2O, dried, and concentrated. The solution was chromatographed on 'Camag' neutral alumina (100–240 mesh). The fraction eluted by $CHCl_3$ was concentrated and separated on thick plates of Kieselgel HF_{254}, using benzene–EtOAc–EtOH (30:30:1). Extraction of the bands and evaporation yielded evonine,[2] m.p. 184° from EtOH, evonoline,[4d] m.p. 118° from EtOH, neoevonine,[4a] m.p. 264° from EtOH, 2-deacetylevonine, and 2,5-bisdeacetylevonine. The first three were identified by comparison of their spectra with those reported in the literature. 2-*Deacetylevonine* (II), m.p. 135° from EtOH, had M^+ 719·241 ($C_{34}H_{41}NO_{16}$ requires: 719·243), λ_{max} (EtOH) 224 (10 020) and 268 nm (3800), ν_{max} (KBr) 3460 (OH), 1740 (ester CO), 1718 (CO), 1573 and 1562 (Ar) $cm.^{-1}$ 2,5-*Bisdeacetylevonine* (III), m.p. 141° from EtOH had M^+ 677·232 ($C_{32}H_{39}NO_{15}$ requires: 677·232), λ_{max} (EtOH) 224 (6240) and 266 nm (2200), ν_{max} (KBr) 3430 (OH), 1735 (ester CO), 1720 (CO), 1580 and 1570 (Ar) cm^{-1}.

5-*Deacetylevonine* p-*bromobenzyl ether*. Evonine (100 mg) in dry dimethylformamide (3 cm^3) was stirred at ambient temp. for 20 hr with *p*-bromobenzyl bromide (100 mg) and silver oxide (400 mg). The product was filtered through neutral alumina and purified by TLC on Silica gel (benzene–EtOAc–EtOH, 30:30:1). Crystallization from EtOH gave 5-*deacetyl evonine* p-*bromobenylether* (IV), m.p. 285° (Found: C, 55·91; H, 5·32; N, 1·42. $C_{41}H_{46}O_{16}$ NBr requires: C, 55·42; H, 5·22; N, 1·25%), M^+ 889, λ_{max} (EtOH) 222 (15 300) and 264 (3160) nm, ν_{max} (KBr) 3565, 1755, 1735, 1723, 1595 and 1570 cm^{-1}. Space group $P2_12_12_1$ from rotation and Weissenberg photographs, $a = 14·85 \pm 0·02$, $b = 16·09 \pm 0·02$, $c = 36·09 \pm 0·04$ Å, $Z = 8$.

6-*Deacetylevonine* p-*Iodobenzyl ether*. By a similar method the corresponding p-*iodobenzyl ether* (V) was prepared, m.p. 289° (Found: C, 52·44; H, 4·76; N, 0·89. $C_{41}H_{46}O_{16}$ NI requires: C, 52·64; H, 4·96; N, 1·5%), M^+ 935, λ_{max} (EtOH) 233 (20 870) and 262 (4180) nm, ν_{max} (KBr) 3555, 1755, 1735, 1715, 1590 and 1565 cm^{-1}, τ4·94 (1H, *bs*, 5-H). Space group $P2_12_12_1$ from rotation and Weissenberg photographs, $a = 14·99 \pm 0·02$, $b = 15·84 \pm 0·02$, $c = 36·40 \pm 0·04$ Å, $Z = 8$.

Acknowledgement—We thank the S.R.C. for support.