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SIX NEW MELAMPOLIDES FROM *TETRAGONOTHECA HELIANTHOIDES*

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Key Word Index—*Tetragonotheca helianthoides*; Compositae; Heliantheae; sesquiterpene lactone; melampolides.

Abstract—Chemical analysis of *Tetragonotheca helianthoides* L. yielded six new melampolide-type sesquiterpene lactones, tetrahelins A–F. All new compounds have the same medium ring skeleton and differ by the ester moieties at C-8 and C-9. Tetrahelin A and B contain the side chain 2-methyl-2,3-diacetoxybutanoate and tetrahelin E 3-hydroxy-3-methylbutanoate. Both ester side chains have previously not been found in sesquiterpene lactones.

INTRODUCTION

The sesquiterpene lactone analysis of two populations of *Tetragonotheca helianthoides* (Compositae, Heliantheae) yielded six new melampolides, which we named tetrahelin A to F. The new compounds are structurally similar to melampolides previously isolated from *Tetragonotheca ludoviciana* [1], *Melampodium longipes* [2], *Polymnia uvedalia* [3] and *P. maculata* [4, 5]. The tetrahelin series is distinguished by ester side chains at C-8 and C-9, several of which are novel. In two instances, tetrahelin B and F, the C-15 represent hydroxymethylene functions.

The structures of the tetrahelins were deduced by comparison of the physical parameters of the natural products and their derivatives with those of known melampolides [1, 4] and extensive NMR spin decoupling experiments of all new compounds.

RESULTS AND DISCUSSION

Tetrahelin A (**1a**), $C_{27}H_{34}O_{12}$, displayed in the 100 MHz NMR spectrum two one-proton doublets at 6.25 ($J = 3.5$ Hz, H-13b) and 5.78 ppm ($J = 3.0$ Hz, H-13a) and a broad one-proton multiplet at 2.80 ppm that are characteristic of α,β-unsaturated γ-lactones. Irradiation of the multiplet at 2.80 ppm affected the doublet of doublets at 6.63 ppm (H-8; $J_{7,8} = 1.5$ Hz, $J_{8,9} = 8.0$ Hz) to a doublet, simplified the H-6 proton of the two overlapping proton signals at 5.05 (H-6) and 4.94 ppm (H-5), and collapsed the two H-13 doublets to singlets. Irradiation of the H-8 signal at 6.63 ppm collapsed a doublet at 5.36 ppm (H-9, $J_{8,9} = 8.0$ Hz) and simplified the H-7 multiplet at 2.80 ppm. Irradiation of H-6 at 5.05 ppm also collapsed the signal at 2.80 ppm and decoupling of the most downfield signal at 6.98 ppm (H-1) affected only the envelope between 2.00 and 3.00 ppm which contains the C-2 methylene proton signals. Other proton absorptions of **1a** resembled the diol derived from uvedalin [3] except that the C-3′ proton signal of the diol appeared as a quartet at 3.8 ppm while the quartet in **1a** occurred at 5.16 ppm beside a doublet at 1.18 ppm and a singlet at 1.53 ppm, suggesting a side chain in **1a** which must be represented by **A**. Indeed, when the three-proton doublet at 1.18 ppm (C-3′-Me) was irradiated the quartet at 5.16 ppm (H-3′, $J_{3',4'} = 6.5$ Hz) collapsed to a singlet. The above NMR data were corroborated by diagnostic MS peaks. Besides a weak M^+ at m/e 550 the base at m/e 272 indicated the loss of acetic acid and the acid **A**($C_9H_{14}O_6$) by McLafferty rearrangements as the major fragmentation. Further peaks at m/e 201 ($C_9H_{13}O_5$, **A′**), 173 ($C_8H_{13}O_4$, **A″**) and 131 ($C_6H_{11}O_3$) supported the presence of side chain **A** in **1a**. Since **1a** exhibited NMR signals nearly identical to those of other melampolides with established structure and stereochemistry [1, 5], structure **1a** is suggested for tetrahelin A. The diol **1b** has also been found in *Tetragonotheca ludoviciana* [1], and its acetylation product is similar to **1a**. However, the NMR spectral peaks for the side chain of **1a** and acetate **1b** have slightly different chemical shifts, which is most likely due to differences in chirality at C-2′ and/or C-3′ in **1a** and the acetate of **1b**. Similar observations have been reported before [1,4,6].

Tetrahelin C (**3**) $C_{28}H_{38}O_{11}$, and *tetrahelin D* (**4**), $C_{25}H_{32}O_{11}$, exhibited NMR spectral parameters which were nearly identical with those for the medium ring portion of **1a**. In addition, NMR signals (Table 1) together with diagnostic MS peaks suggested the presence of ester side chains **B** (m/e 159, $C_7H_{11}O_4$ (**B$_1$**); m/e 131, $C_6H_{11}O_3$ (**B$_2$**)) and **C** (m/e 85, C_5H_9O (**C$_1$**); m/e 57, C_4H_9 (**C$_2$**)) in **3** and its acetate and **B** in **4**. Other significant MS peaks diagnostic for the ester moiety **B** appeared at m/e 71 and 89 which must be formed by fragmentations of **B** involving cleavage between C-1′ and C-2′ as outlined previously [6].

Tetrahelin E (**5**), $C_{28}H_{38}O_{12}$, exhibited NMR signals nearly identical with **4** except that instead of an acetate signal in **4**, compound **5** showed a two-proton singlet at 2.44 ppm together with a six-proton singlet at 1.22 ppm. The NMR parameters and the MS data were in good agreement with a 3-hydroxy-3-methylbutyrate moiety (**D**). MS peaks at *m/e* 83 [$(Me)_2C{=}CH{-}CO^+$, **D_1**-H_2O], 59 (**D_3**) and 55 (C_4H_7 by loss of H_2O and C-1′-2′ cleavage) are diagnostic of side chain **D**.

Treatment of **5** with acetic anhydride in pyridine provided a complex mixture of acetylation products, the major constituent of which was isolated by preparative TLC. The IR, NMR and MS spectral data indicated formation of a compound identical with **4**, that is replacement of side chain **D** by acetate. Reactions of this type seem to preferentially occur at the activated allylic C-9 position of melampolides suggesting the attachment of **D** to C-9 in **5**. By analogy it is assumed that in **1a** and **3** the acetates are also attached to C-9.

Tetrahelin B (**2a**), $C_{27}H_{34}O_{13}$, and *tetrahelin F* (**6a**), $C_{25}H_{32}O_{12}$, showed NMR spectral parameters that differed from those of **1a** most noticeably by the presence of a pair of one-proton doublets (4.34 and 4.55 ppm in **2a**) instead of the methyl singlet at 1.98 ppm in **1a**. This pair of doublets ($J_{15a,15b} = 14.0$ Hz) was assigned to the hydroxymethylene (C-15) at C-4. The presence of a hydroxyl group at C-15 produced a downfield shift of the C-6β-hydrogen from 5.05 in **1a** to 5.36 ppm in **2a**. Detailed NMR decoupling experiments on tetrahelin B and F led to the assignments summarized in Table 1 and are in full agreement with structures **2a** and **6a**.

MnO_2 oxidation of **2a** produced the aldehyde **2b**. The NMR spectrum of **2b** exhibited an aldehyde singlet at 10.20 ppm (H-15), and a doublet at 6.11 ppm (H-5), the NMR chemical shift of which indicated a *trans* 4,5-double bond [7]. Furthermore, the introduction of a C-15 aldehyde carboxyl exhibited a deshielding effect on the C-6β-hydrogen appearing at 5.77 ppm in **2b**. This is in full accord with an orientation of C-15 above the medium ring plane which is typical for melampolide conformations [8]. The mass spectral fragmentations fully supported the above NMR assignments (see Experimental). Diagnostic NMR and MS absorptions indicated that **6a** differed from **2a** by the presence of side chain **B** instead of **A**. The chemical shifts of H-6 (5.61 ppm) and H-9 (5.58 ppm) in **6a** compared to the signals in **2a** (H-6, 5.36 ppm and

Table 1. ¹H NMR parameters* of tetrahelin A (**1a**), B (**2a**), C (**3**), D (**4**), E (**5a**), and F (**6a**) and derivatives

	1a	**2a**	**2b**	**3**‡	**4**	**5**§	**6a**	**6b**
H-1	6.98*dd* (9.5,7.5)	7.00*dd* (9.5,7.5)	7.01*dd* (8.5,11.5)	7.00*dd* (7.5,10.0)	7.01*dd* (7.5,10.0)	7.02*dd* (7.5,10.0)	7.02*dd* (7.5,10.0)	7.02*dd* (7.5,10)
H-5	4.94*d*† (8.5)	5.03*d* (10.0)	6.11*d* (10.5)	4.94*d*† (10.0)	4.93*d*† (10.0)	4.95*d*† (10.0)	5.03*d* (10.0)	5.12*d* (10)
H-6	5.05†	5.36*dd* (10.0,10.5)	5.77*dd* (10.0,10.5)	5.05†	5.01†	5.05†	5.61*dd* (10.0,9.5)	5.28*dd* (10,10)
H-7	2.80*m*	2.80*m*	2.91*m*	2.83*m*	2.80*m*	2.83*m*	2.83*m*	2.80*m*
H-8	6.63*dd* (1.5,8.0)	6.62*dd* (1.5,8.0)	6.66*dd* (1.0,8.0)	6.71*dd* (1.0,8.0)	6.71*dd* (1.5,8.5)	6.68*dd* (1.0,8.5)	6.62*dd* (1.0,8.5)	6.71*dd* (1.5,8.0)
H-9	5.36*d* (8.0)	5.43*d* (8.0)	5.12*d* (8.0)	5.35*d* (8.0)	5.38*d* (8.5)	5.40*d* (8.5)	5.58*d* (8.5)	5.40*d* (8.0)
H-13a	5.78*d* (3.0)	5.80*d* (3.0)	5.92*d* (3.0)	5.79*d* (3.0)	5.78*d* (3.0)	5.77*d* (3.0)	5.81*d* (3.0)	5.83*d* (3.0)
H-13b	6.25*d* (3.5)	6.26*d* (3.5)	6.35*d* (3.5)	6.28*d* (3.5)	6.27*d* (3.5)	6.26*d* (3.5)	6.28*d* (3.5)	6.31*d* (3.5)
H-15	1.98*brs* [3]	(a)4.43*d*(14.0) (b)4.55*d*(14.0)	10.20	2.01[3]	2.00[3]	2.01[3]	4.49[2]	(a)4.78*d*(13) (b)5.12*d*(13)
COOMe	3.78	3.79	3.79	3.79	3.79	3.78	3.79	3.81
H-3′	5.16*q* (6.5)	5.51*q* (6.5)	5.23*q* (6.5)	5.06*q* (6.5)	5.06*q* (6.5)	5.06*q* (6.5)	5.18*t* (6.5)	5.08*q* (6.5)
C-3′-Me	1.18*d* (6.5)	1.18*d* (6.5)	1.17*d* (6.5)	1.12*d* (6.5)	1.12*d* (6.5)	1.12*d* (6.5)	1.08*d* (6.5)	1.18*d* (6.5)
C-2′-Me	1.53	1.57	1.52	1.27	1.27	1.27	1.27	1.32
OAc	2.01 2.03 2.04	2.06 2.06	1.99 2.01 2.06	2.03	1.97 2.04	2.03	1.96 2.06	1.96 2.13

*Spectra were run at ambient temperatures in $CDCl_3$ at 100 MHz and TMS was used as internal standard. Values are recorded in ppm relative to TMS. Signals are designated as follows: singlets are unmarked; doublet, *d*; triplet, *t*; quartet, *q*; pentet, *p*; multiplet, *m*, whose center is given; broad, *br*. Figures in parentheses are coupling constants or line separations in hertz. Numbers in brackets indicate number of protons.

†Partially obscured by overlapping signals.

‡The C-2″-Me absorption at 1.04*d* (7.0) and C-4″-Me at 0.82 ppm.

§H-2″ represents a two-proton singlet at 2.44 ppm; the two C-3″-Me appear as a singlet at 1.22 ppm.

H-9, 5.43 ppm) suggests deshielding of the two protons caused by the C-2′-acetate carbonyl in **2a**. The effect of the C-2′ acetate upon the β-oriented H-6 and H-9 suggested that side chains **A** and **B** in **2a** and **6a**, respectively have to be β-attached to C-8 to sterically allow the observed effect on H-6 and H-9. An α-attachment of the two ester functions to C-9 would, due to a steric remoteness, not be expected to exhibit an influence on H-6.

On the basis of the great similarity of the NMR and CD parameters of the six new tetrahelins with uvedalin [3], a compound of established absolute configuration by correlation with enhydrin [9], it appears that **1a** to **6a** have configurations and conformations around the medium ring as established for the other melampolides [1, 3, 9].

EXPERIMENTAL

IR spectra in $CHCl_3$ and UV and CD in MeOH. Low resolution MS: 70 eV, direct probe. *Tetragonotheca helianthoides* (F. F. Wellington, collected in 1976 from U.S.A.: Georgia, Callaway Gardens, GA.) dried leaves and stems (521 g) were extracted in 3 l. $CHCl_3$. Standard work-up [10] provided 12.8 g of crude syrup which was chromatographed over 250 g Si gel, first using CH_2Cl_2 followed by CH_2Cl_2–Me_2CO mixtures as eluents with increasing amounts of Me_2CO (19:1, 9:1, 4:1, etc.) taking 20 ml fractions. Fractions 4–11 yielded 150 mg of **1a**, and fractions 51–59 contained 125 mg of **2a**. A second collection of *T. helianthoides* (Urbatch No. 2750; Mississippi, Lamar Co., 13 July 1976, voucher deposited at LSU) was extracted and chromatographed as described above. Fractions 3–15 contained the acetylenic alcohol (**7**), fractions 32–41 consisted of 100 mg of **1a**, and fractions 75–89 contained 150 mg of **2a**. Rechromatography of fractions 52–65 over 50 g Si gel gave 50 mg of **3** and 75 mg of **4**. Rechromatography of fractions 89–104 provided 120 mg of **5**, and 85 mg of **6a**.

Tetrahelin A (**1a**). Gum, UV λ_{max} 205 nm (ε 1.1×10^4); CD (*c* 1.6×10^{-4}, MeOH); $[\theta]_{214}$ -7.7×10^4, $[\theta]_{260}$ -2.6×10^3; IR ($CHCl_3$) cm^{-1}: 1765 (γ-lactone), 1745, 1740, 1735, 1715 (esters), 1670, 1650 (double bonds); MS *m/e* (rel. int.) assignment: 550 (0.5) M^+, 490 (1.0) $M-C_2H_4O_2$, 464 (1.8) $M-C_2H_2O-CH_4O$, 430 (6.8) $M-C_2H_4O_2-C_2H_4O_2$, 404 (0.6) $M-C_2H_2O-CH_4O-C_2H_4O_2$, 333 (2.7) $M-C_9H_{13}O_6$, 332 (1.2) $M-C_9H_{14}O_6$, 272 (100.0) $M-C_9H_{13}O_6$-$C_2H_4O_2$, 240 (13.8) $M-C_9H_{13}O_6-C_2H_4O_2-MeOH$, 201 (24.5) $C_9H_{13}O_5$, 173 (7.5) $C_8H_{13}O_4$, 159 (21.8) $C_7H_{11}O_4$, 131 (53.3) $C_6H_{11}O_3$, 43 (21.7) C_2H_3O. (Calc. for $C_{27}H_{34}O_{12}$: 550.2048. Found: (MS) 550.2049).

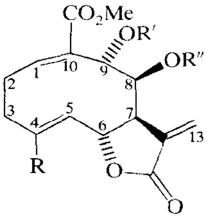
Tetrahelin B (**2a**). Gum, UV λ_{max} 205 nm (ε 1.0×10^4); CD (*c* 5.8×10^{-4}, MeOH); $[\theta]_{215}$ -5.6×10^4; IR ($CHCl_3$) cm^{-1}: 3500 (OH), 1760 (γ-lactone), 1740, 1735, 1730, 1715 (esters), 1680, 1650 (double bonds); MS *m/e* (rel. int.) assignments: 566 (0.5) M^+, 478 (1.0) $M-C_2H_2O-C_2H_4O$, 446 (2.2) $M-C_2H_4O_2-C_2H_4O_2$, 354 (4.9) $M-3(C_2H_4O_2)-MeOH$, 349 (1.7) $M-C_9H_{13}O_6$, 348 (1.5) $M-C_9H_{14}O_6$, 330 (16.3) $M-C_9H_{14}O_6-H_2O$, 307 (2.9) $M-C_2H_2O-C_9H_{13}O_6$, 306 (1.2) $M-C_2H_2O-C_9H_{14}O_6$, 289 (19.0) $M-C_2H_4O_2-C_9H_{13}O_6$, 288 (24.6) $M-C_2H_4O_2-C_9H_{14}O_6$, 271 (13.4) $M-C_2H_4O_2-H_2O-C_9H_{13}O_6$, 270 (42.6) $M-C_2H_4O_2—H_2O—C_2H_4O_2$, 256 (20.7)$M-C_2H_4O_2-C_9H_{14}O_6-MeOH$, 201 (50.1) $C_9H_{13}O_5$, 173 (11.4) $C_8H_{13}O_4$, 159 (38.9) $C_7H_{11}O_4$, 131 (100.0) $C_6H_{11}O_3$, 43 (93.2) C_2H_3O. (Calc. for $C_{27}H_{34}O_{13}$: 566.1996. Found: (MS) 566.2044). Compound **2a** (50 mg) was oxidized using 300 mg of activated MnO_2 in 10 ml $CHCl_3$ for 11 hr, yielding 30 mg of **2b** (gum), IR ($CHCl_3$) cm^{-1}: 1765 (γ-lactone), 1750, 1740, 1725, 1710 (esters), 1680 (α, β-unsaturated aliphatic aldehyde), 1660, 1640 (double bonds); MS, *m/e* (rel. int.) assignments: 564 (6.1) M^+, 505 (1.9) $M-C_2H_3O_2$, 478 (4.2) $M-C_2H_2O-C_2H_4O$, 445 (4.2) $M-C_2H_4O_2-C_2H_3O_2$, 418 (9.9) $M-C_2H_4O_2-C_2H_2O-C_2H_4O$, 376 (3.8) $M-C_2H_4O_2-C_2H_2O-C_2H_2O-C_2H_4O$, 347 (14.6) $M-C_9H_{13}O_6$, 346 (9.9) $M-C_9H_{14}O_6$, 305 (10.5) $M-C_2H_2O-C_9H_{13}O_6$, 304 (4.4) $M-C_2H_2O-C_9H_{14}O_6$, 286 (26.4) $M-C_9H_{14}O_6-C_2H_4O_2$, 257 (21.9) $M-C_9H_{14}O_6-C_2H_4O_2-CHO$, 201 (34.0) $C_9H_{13}O_5$, 173 (11.4) $C_8H_{13}O_4$, 159 (40.9) $C_7H_{11}O_4$, 131 (100.0) $C_6H_{11}O_3$, 43 (21.1) C_2H_3O.

Tetrahelin C (**3**). Gum, UV λ_{max} 205 nm (ε 1.6×10^4); CD (*c* 1.1×10^4 MeOH); $[\theta]_{214}$ -1.2×10^5, $[\theta]_{260}$ -3.6×10^3; IR ($CHCl_3$) cm^{-1}: 3500 (OH), 1770 (γ-lactone), 1745, 1740, 1720 (esters), 1670, 1630 (double bonds); MS *m/e* (rel. int.) assignments: 550 (0.6) M^+, 532 (0.3) $M-H_2O$, 490 (0.4) $M-C_2H_4O_2$, 464 (3.1) $M-C_2H_2O-C_2H_4O$, 448 (0.4) $M-C_5H_{10}O_2$, 430 (1.9) $M-C_5H_{10}O_2-H_2O$, 362 (1.3) $M-C_5H_{10}O_2-C_2H_2O-C_2H_4O$, 272 (100.0) $M-C_5H_{10}O_2-C_7H_{12}O_5$, 240 (13.9) $M-C_5H_{10}O_2-C_7H_{12}O_5-MeOH$, 159 (11.5) $C_7H_{11}O_4$, 131 (35.7) $C_6H_{11}O_3$, 89 (22.2) $C_4H_9O_2$, 85 (47.5) C_5H_9O, 71 (16.0), 57 (51.5) C_4H_9, 43 (27.7) C_2H_3O. (Calc. for $C_{28}H_{38}O_{11}$: 550.2412. Found: (MS) 550.2407).

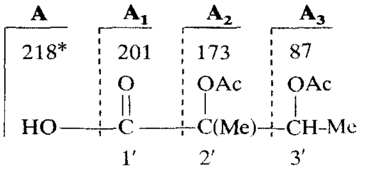
Tetrahelin D (**4**). Gum, UV λ_{max} 205 nm (ε 1.4×10^4); CD (*c* 1.8×10^4, MeOH); $[\theta]_{214}$ -8.8×10^4, $[\theta]_{261}$ -4.5×10^3; IR ($CHCl_3$) cm^{-1}: 3500 (OH), 1765 (γ-lactone), 1740, 1730, 1720 (esters), 1670, 1630 (double bonds); MS *m/e* (rel. int.) assignments: 508 (0.8) M^+, 490 (0.7) $M-H_2O$, 449 (0.7) $M-C_2H_3O_2$, 448 (0.7) $M-C_2H_4O_2$, 430 (2.3) $M-C_2H_4O_2-H_2O$, 422 (4.7) $M-C_2H_2O-C_2H_4O$, 362 (1.3) $M-C_2H_4O_2-C_2H_2O-C_2H_4O$, 291 (8.7) $M-C_7H_{11}O_5-C_2H_2O$, 290 (5.2) M-$C_7H_{12}O_5-C_2H_2O$, 272 (100.0) $M-C_2H_4O_2-C_7H_{12}O_5$, 240 (17.2) $M-C_7H_{12}O_5-C_2H_4O_2-MeOH$, 159 (11.1) $C_7H_{11}O_4$, 131 (37.1) $C_6H_{11}O_3$, 89 (33.0) $C_4H_9O_2$, 71 (30.2), 43 (58.2) C_2H_3O. (Calc. for $C_{25}H_{32}O_{11}$: 508.1943. Found: (MS) 508.1957).

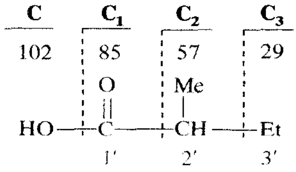
Tetrahelin E (**5**). Gum, UV λ_{max} 205 nm (ε 1.9×10^4); CD (*c* 1.9×10^4, MeOH); $[\theta]_{215}$ -1.2×10^5, $[\theta]_{263}$ -5.1×10^3; IR ($CHCl_3$) cm^{-1}: 3480 (OH), 1765 (λ-lactone), 1740, 1735, 1720 (esters), 1655, 1630 (double bonds); MS *m/e* (rel. int.) assignments: 566 (0.4) M^+, 548 (0.5) $M-H_2O$, 480 (0.7) $M-C_2H_2O-C_2H_4O$, 448 (0.8) $M-C_5H_{10}O_3$, 430 (1.1) $M-C_5H_{10}O_3-H_2O$, 390 (0.5) $M-C_7H_{12}O_5$, 362 (3.8) $M-C_5H_{10}O_3-C_2H_2O-C_2H_4O$, 272 (100.0) $M-C_5H_{10}O_3-C_7H_{12}O_5$, 240 (9.6) $M-C_5H_{10}O_3-C_7H_{12}O_5-MeOH$, 159 (6.9) $C_7H_{11}O_4$, 131 (15.2) $C_6H_{11}O_3$, 89 (17.9) $C_4H_9O_2$, 71 (30.2), 59 (12.3) C_3H_7O, 55 (5.8) C_4H_7, 43 (25.3) C_2H_3O. (Calc. for $C_{28}H_{38}O_{12}$: 566.5380. Found: (MS) 566.2519). Acetylation of 60 mg of **5** in Py–Ac_2O for 2 days yielded a mixture of products. Preparative TLC of this mixture in $CHCl_3$–Me_2CO (9:1) provided 20 mg of a gum, which was shown to be identical with **4** by NMR, IR and MS.

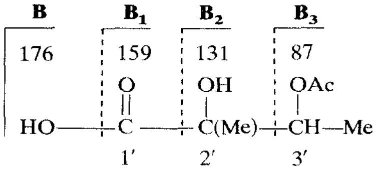
Tetrahelin F (**6a**). Gum, UV λ_{max} 205 nm (ε 1.2×10^4); CD (*c* 9.5×10^{-5}, MeOH); $[\theta]_{213}$ -5.2×10^4, $[\theta]_{261}$ -1.0×10^3; IR ($CHCl_3$) cm^{-1}: 3470 (OH) 1765 (γ-lactone), 1745, 1740, 1720 (esters), 1670, 1625 (double bonds); MS, *m/e* (rel. int.) assignments: 524 (not observed) M^+, 438 (2.2) $M-C_2H_2O-C_2H_4O$, 420 (2.2) $M-C_2H_2O-H_2O-C_2H_4O$, 391 (4.5), 348 (3.7) $M-C_7H_{12}O_5$, 306 (11.2) $M-C_7H_{12}O_5-C_2H_2O$, 289 (25.4) $M-C_7H_{12}O_5-C_2H_3O_2$, 288 (21.6) $M-C_7H_{12}O_5-C_2H_4O_2$, 270 (37.3) $M-C_7H_{12}O_5-C_2H_4O_2-H_2O$, 256 (28.4) $M-C_7H_{12}O_5-C_2H_4O_2-MeOH$, 159 (15.7) $C_7H_{11}O_4$, 131 (77·6) $C_6H_{11}O_3$, 89 (71.6) $C_4H_9O_2$, 71

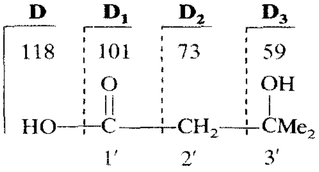


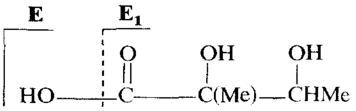
	R	R′	R″
Tetrahelin A (**1a**)	Me	Ac	**A**$_1$
(**1b**)	Me	Ac	**E**$_1$
Tetrahelin B (**2a**)	CH_2OH	Ac	**A**$_1$
(**2b**)	CHO	Ac	**A**$_1$
Tetrahelin C (**3**)	Me	**C**$_1$	**B**$_1$
Tetrahelin D (**4**)	Me	Ac	**B**$_1$
Tetrahelin E (**5**)	Me	**D**$_1$	**B**$_1$
Tetrahelin F (**6a**)	CH_2OH	Ac	**B**$_1$
(**6b**)	CH_2OAc	Ac	**B**$_1$

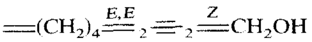












$$=(CH_2)_4\overset{E,E}{=\!=}_2\equiv_2\overset{Z}{=\!=}CH_2OH$$

7 [1]

*Mass units of MS fragment.

(59.7), 43 (31.6) C_2H_3O. (Calc for $C_{21}H_{26}O_{10}$: 438.1524. Found: (MS) 438.1535).

Acetate **6b**. 25 mg of **6a** were treated for 4 hr with Ac_2O–Py yielding 24 mg of **6b**, gum (Table 1).

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