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TWO NATURALLY OCCURRING ACYCLIC DITERPENE AND NORDITERPENE ALDEHYDES FROM *TETRAGONIA TETRAGONOIDES*

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Key Word Index—*Tetragonia tetragonoides*; Aizoaceae; leaves; stems; 6,10,14-trimethyl-2-methylene-pentadecanal; (2*E*)-3,7,11,15-tetramethyl-2-hexadecenal; neophytadiene; phytol; fatty acids; fatty acid methyl esters; ferulic acids and their methyl esters.

Abstract—In addition to neophytadiene, phytol, methyl (2*E*)- and (2*Z*)-3-(4-hydroxy-3-methoxyphenyl) propenates, fatty acid methyl esters and fatty acids, a new acyclic diterpene aldehyde and a new norditerpene aldehyde were isolated from the leaves of *Tetragonia tetragonoides*. The structures of these new aldehydes were shown to be 6,10,14-trimethyl-2-methylene-pentadecanal and (2*E*)-3,7,11,15-tetramethyl-hexadecenal. (2*E*)-3-(4-Hydroxy-3-methoxyphenyl) propenic acid accompanied with very small amounts of its *cis* isomer was isolated from the ethyl acetate-soluble fraction of the leaves and the stems.

INTRODUCTION

The leaves of *Tetragonia tetragonoides* (Japanese name: Tsuruna) are used as a substitute for vegetables in a certain district in Japan and are said to be anti-carcinogenic to stomach cancer. However, there have been no reports on the chemical constituents of this plant. We have now examined the chemical constituents of the leaves and the stems of the plant.

RESULTS AND DISCUSSION

Isolation and identification of the chemical constituents

The hexane soluble fraction of the methanol extract of the leaves gave the two new naturally occurring aldehydes, 6,10,14-trimethyl-2-methylene-pentadecanal (**2**) and (2*E*)-3, 7, 11, 15-tetramethyl-2-hexadecenal (**3**), in addition to neophytadiene (**1**), phytol (**4**), methyl (2*E*)- and (2*Z*)-3-(4-hydroxy-3-methoxyphenyl) propenates (methyl *trans*- and *cis*-ferulates) (**5** and **6**), fatty acid methyl esters and fatty acids. These constituents with the exception of **1–3**, were also found in the hexane-soluble fraction of the stems. (2*E*)- and (2*Z*)-3-(4-Hydroxy-3-methoxyphenyl) propenic acids (*trans*- and *cis*-ferulic acids) (**7** and **8**) were found in the ethyl acetate-soluble fraction of the leaves and the stems. The amounts (% fr. wt) of these compounds in leaves and stems were as follows. Leaves: 0.00002 **1**, 0.00056 **2**, 0.00007 **3**, 0.00212 **4**, 0.00021 **5**, 0.00001 **6**, 0.00007 **7**, trace **8**, 0.01645 fatty acids, 0.01026 fatty acid methyl esters; stems: 0.00006 **4**, 0.00012 **5**, 0.00002 **6**, 0.00005 **7**, trace **8**, 0.00111 fatty acids, 0.00886 fatty acid methyl esters. The compositions of the fatty acids and fatty acid methyl esters are given in Table 1. Since it has been observed that exposure of the *trans* form of cinnamic acid derivatives to light resulted in the formation of their *cis* isomers [1, 2], the occurrence of the *cis* forms of ferulic acid (**6**) and its methyl ester (**8**) in very small amounts can probably be ascribed to the geometrical isomerization of the *trans* isomers by unavoidable exposure to light in the courses of the isolation and identification of the constituents.

6,10,14-*Trimethyl-2-methylene-pentadecanal* (**2**). High resolution mass spectrometry ($[M]^+ = 280.2801$) gave the molecular formula as $C_{19}H_{36}O$. ^{13}C and ^{1}H NMR signals at δ_c 194.6 and δ 9.55 (1H, *s*, $-(CHO)\,C{=}C\langle$) indicated the presence of an aldehyde group, and signals at δ_c 150.7 and 133.5 and δ 6.10, the presence of a terminal methylene. The presence of the aldehyde group was confirmed by the fact that sodium borohydride reduction followed by acetylation gave a primary acetate [^{1}H NMR: δ 2.07 (3H, *s*, –CO-Me) and δ 4.51 (2H, *s*, $-CH_2-OAc$)]. IR absorption bands at 1692 and 1627 cm^{-1} indicated that the aldehydic carbonyl group was conjugated with the terminal methylene. The appearance of the fragment ions assigned to $[CH_2(CHO)C{=}CH_2 + H]^+$, $[CH_2(CHO)C{=}CH_2]^+$ and $[(CHO)C{=}CH_2]^+$ in the high resolution mass spectrum indicated clearly not only the conjugation of the terminal methylene with the aldehydic carbonyl group, but also the presence of a 2-methylenepropanal group. Comparison of the ^{13}C NMR chemical shifts of **2** with those of (2*E*)-3,7,11,15-tetramethyl-2-hexadecen-1-ol (phytol) (**4**) indicated that **2** possessed three isoprene units linked head to tail with a 2-methylenepropanal group linked to the end of the isoprene chain. All the above data led to the establishment of the structure of **2** as 6,10,14-trimethyl-2-methylene-pentadecanal.

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Table 1. Fatty acid compositions of the free acids and esters in the leaves and the stems of *T. tetragonoides*

	% composition of fatty acids						
	14 : 0	16 : 0	18 : 0	18 : 1	18 : 2	18 : 3	Unknown
Leaves							
Free fatty acids	1.7	17.6	0.9	9.7	11.0	56.7	2.4
Fatty acid methyl esters	0.4	14.0	0.4	11.0	13.1	57.5	3.6
Stems							
Free fatty acids	0.9	40.8	1.9	15.7	30.8	6.3	3.6
Fatty acid methyl esters	1.3	27.6	1.0	11.6	36.6	20.9	1.0

(2*E*)-3,7,11,15-*Tetramethyl-2-hexadecenal* (**3**). The molecular formula of **3** was found to be $C_{20}H_{38}O$ (high resolution mass spectrometry: $[M]^+$ at *m/z* 294.2933). The ^1H NMR signal at δ 9.98 (1H, *d*, $J = 8$ Hz, =CH–C$\underline{H}$O) indicated the presence of an aldehyde group in **3**. Furthermore, the IR absorption bands at 1678 and 1631 cm^{-1} suggested that the aldehydic carbonyl group was conjugated with a double bond having an olefinic proton. This was confirmed by the ^1H NMR signal at δ 5.88 (1H, *d*, $J = 8$ Hz, $>$C=C$\underline{H}$–CHO). Two mass spectral fragment ions (*m/z* 84.0594 and 83.0484) assigned to $[CH_2(Me)C{=}CH(CHO) + H]^+$ and $[CH_2(Me)C{=}CH(CHO)]^+$ respectively indicated the conjugated grouping was part of a 3-methyl-2-butenol group. The other mass fragment patterns were similar to those of (2*E*)-3, 7, 11, 15-tetramethyl-2-hexadecen-1-ol (phytol) (**4**). These spectral data indicated that **3** possessed three isoprene units linked head to tail with a 3-methyl-2-butenal group bound to the end of this isoprene chain. The structure of **3** was finally elucidated by comparison of the spectral data with those of (2*E*)-3, 7, 11, 15-tetramethyl-2-hexadecenal (phytal), which was prepared from **4** by manganese dioxide oxidation.

EXPERIMENTAL

NMR: TMS as int. standard, 60 and 90 MHz for ^1H ($CDCl_3$) and 22.6 MHz for ^{13}C ($CDCl_3$); MS: direct inlet, 70 eV ionization; GLC (FID): glass column (3 mm × 2 m) packed with 15% DEGS and 2% OV-17 on Chromosorb W (80–100 mesh); HPLC: stainless steel column (4.6 mm × 30 cm) packed with PS-DVB (Fine Gel-101) and Si ODS (TSK Gel-410K), column effluent monitored at 254 nm; TLC (0.25 mm) and prep. TLC (0.75 mm): Si gel (Merck; Type 60, GF_{254}). The compounds on the plate were visualized as coloured spots by spraying with HNO_3–H_2SO_4 (1 : 19) and then heating.

Materials. The leaves (42.5 kg) and the stems (47.0 kg) of *T. tetragonoides* Kunze were collected in May at the coast of the island located at the Seto-naikai in the vicinity of Hiroshima City.

Extraction and isolation. The respective parts of the plant were cut into pieces and immersed in MeOH for 3 months at room temp. in the dark. The MeOH soln, after concn at red. pres., was extracted with hexane followed by EtOAc. The hexane-soluble fraction was treated with 5% $NaHCO_3$ followed 5% NaOH and separated into a neutral, a phenolic and an acidic portion. The neutral and the phenolic portions were subjected to prep. TLC, $AgNO_3$-impregnated prep. TLC or prep. TLC with continuous development. The neutral portion gave compounds **1**–**4** and fatty acid methyl esters and the phenolic portion gave compounds **5** and **6**. The acidic portion was methylated with CH_2N_2 and then subjected to co-GLC with authentic samples. The EtOAc-soluble fraction was subjected to prep. TLC with continuous development to give compounds **7** and **8**. The purity of these compounds was examined by HPLC. As far as possible, the isolation and identification procedures were carried out in the dark.

6,10,14-*Trimethyl-2-methylene-pentadecanal* (**2**) ($C_{19}H_{36}O$). This aldehyde was isolated by prep. TLC with hexane–EtOAc (9 : 1) as a colourless oil; MS *m/z*: 280.2801 (Calc. for $C_{19}H_{36}O$, 280.2774), 84.0578 (base, C_5H_8O, 84.0575), 70.0422 (C_4H_6O, 70.0418), 69.0344 (C_4H_5O, 69.0348); IR ν_{max}^{film} cm^{-1}: 1692 (–CHO), 1627 (C=C); ^1H NMR: δ 9.55 (1H, *s*, –CHO), 6.10 (2H, *d*, $J = 24$ Hz, $>$C=CH_2); ^{13}C NMR: δ_c 194.6 (*d*, –CHO), 150.7 and 133.5 (*t* and *s*, $>$C=CH_2), 37.4 (*t*, –CH_2– × 3), 39.4, 36.7, 28.0, 25.3, 24.9 and 24.5 (*t*, –CH_2– × 6), 32.7 (*d*, $>$CH– × 2), 28.0 (*d*, $>$CH–), 22.7 (*q*, Me × 2), 19.7 (*q*, Me × 2); UV λ_{max}^{EtOH} nm (log ϵ): 215 (3.61).

$NaBH_4$ *reduction of* **2**. To a soln of **2** (15 mg) in MeOH (5 ml), a suspension of $NaBH_4$ (20 mg) in MeOH (5 ml) was added. The mixture was stirred for 1.5 hr at 5°, acidified (5% HCl) and extracted with Et_2O. The Et_2O extract was subjected to prep. TLC with hexane–EtOAc (17 ; 3) to give a reduction product (9 mg), liquid; IR ν_{max}^{film} cm^{-1}: 3210, 1025 (OH), 3075, 1646, 895 (C=C); ^1H NMR: δ 4.95 (2H, *d*, $J = 12.4$ Hz, $>$C=CH_2), 4.06 (2H, *br s*, –C$\underline{H}_2$–OH). Acetylation of the reduction product with Ac_2O (2 ml)–pyridine (1 ml) gave a monoacetate (11 mg); MS *m/z* (rel. int.): 324 $[M]^+$ (5), 43 (100); IR ν_{max}^{film} cm^{-1}: 3083, 1662 and 907 (C=CH_2), 1746 (–OCOMe); ^1H NMR: δ 2.07 (3H, *s*, –CO–Me), 4.51 (2H, *s*, –CH_2–OAc), 4.96 (2H, *d*, $J = 6.4$ Hz, $>$C=CH_2).

(2E)-3,7,11,15-*Tetramethyl-2-hexadecenal* (**3**) ($C_{20}H_{38}O$). **3** was isolated by prep. TLC with hexane–Et_2O (49 : 1) for 6 hr as a colourless oil; MS *m/z*: 294.2933 (calc. for $C_{20}H_{38}O$: 294.2921), 84.0594 (base, C_5H_8O: 84.0574), 83.0484 (C_5H_7O, 83.0496); IR ν_{max}^{film} cm^{-1}: 1678 (–CHO), 1631 (C=C); ^1H NMR: δ 2.16 [3H, *s*, C$\underline{H}_3$C=C(CHO)–], 5.88 (1H, *d*, $J = 8$ Hz, =C$\underline{H}$–CHO), 9.98 (1H, *d*, $J = 8$ Hz, =CH–C$\underline{H}$O); UV λ_{max}^{EtOH} nm (log ϵ): 236 (4.20). Identity of **3** with phytal was confirmed by direct comparison (TLC, IR and ^1H NMR) with phytal derived from compound **4** by oxidation with active MnO_2.

Identification of the other constituents. (i) 3-Methylene-

7,11,15-trimethyl-hexadec-1-ene (neophytadiene) (**1**) ($C_{20}H_{38}$), liquid; MS *m/z*: 278.2953 (calc. for $C_{20}H_{38}$: 278.2970), 68.0625 (base, C_5H_8: 68.0625)[3]; IR ν_{max}^{film} cm^{-1}: 3090 and 886 $({>}C{=}CH_2)$, 1594 (conjugated C=C), 989 $(-CH{=}CH_2)$[3]; ^1H NMR: δ 4.98 (2H, *s*, ${>}C{=}CH_2$), 5.21 (2H, *d*, $J = 18$ Hz, $-CH{=}C\underline{H}_2$), 6.29–6.49 (3H, ABX-type, $J = 11$ and 17 Hz); UV λ_{max}^{EtOH} nm (log ϵ): 224 (3.99). (ii) (2*E*)-3,7,11,15-Tetramethyl-2-hexadecen-1-ol (phytol) (**4**) ($C_{20}H_{40}O$), liquid; MS *m/z* (rel. int.): 296 $[M]^+$ (3), 278 $[M - H_2O]^+$ (3), 71 (100); IR ν_{max}^{film} cm^{-1}: 3354 (OH), 1662 (C=C); ^1H NMR: δ 1.67 (3H, *s*, ${>}C{=}CMe-$), 4.14 (2H, *d*, $J = 7$ Hz, $=CH-C\underline{H}_2-OH$), 5.64 (1H, *t*, $J = 7$ Hz, $=C\underline{H}-CH_2-OH$); ^{13}C NMR: δ_c 140.2 and 123.4 (C=C), 59.4 $({>}C{=}CH-\underline{C}H_2OH)$, 39.9 $(-\underline{C}H_2-C{=}C{<})$, 16.2 $(-(\underline{C}H_3)C{=}C{<})$. Confirmation of **4** was by direct comparison (TLC, IR, ^1H NMR and MS) with a known sample[4]. (iii) Methyl (2*E*)-3-(4-hydroxy-3-methoxyphenyl) propenate (methyl *trans*-ferulate) (**5**) ($C_{11}H_{12}O_4$), liquid; MS *m/z* 208.0710 (calc. for $C_{11}H_{12}O_4$: 208.0734), 177.0534 (base, $C_{10}H_9O_3$: 177.0550); IR ν_{max}^{film} cm^{-1}: 3400 (OH), 1632 (C=C), 1697 (–CO–O–), 1620, 1513 (arom. C=C), 983 (*trans* –CH=CH–); ^1H NMR: δ 3.76 (3H, *s*, –OMe), 3.86 (3H, *s*, –COOMe), 6.00 (1H, *br*, OH), 6.23 and 7.57 (2H, AB *q*, $J = 16$ Hz, *trans* –CH=CH–), and 7.04 and 7.06 (2H and 1H, *d*, $J = 4$ Hz and *br s*, arom. –CH=CH– and $-CH{=}C{<}$). The purity of **5** was examined by HPLC on PS-DVB with *iso*-PrOH–hexane (1 : 49) as mobile phase and GLC at 160° on OV-17. Acetylation of **5** (25 mg) with Ac_2O (3 ml)–pyridine (2 ml) gave an acetate (23 mg), mp 118.5–119.5°; Found C, 61.91; H, 5.62%, which was identified by comparison (mp, UV, MS, IR and ^1H NMR) with those described in the lit.[5]. (iv) Methyl (2*Z*)-3-(4-hydroxy-3-methoxyphenyl) propenate (methyl *cis*-ferulate) (**6**) ($C_{11}H_{12}O_4$), liquid; MS *m/z* (rel. int.): 208 $[M]^+$ (17), 78 (100); IR ν_{max}^{film} cm^{-1}: 3420 (OH), 1710 (–CO–O–), 1628 (C=C), 1591 and 1515 (arom. C=C), 706 (*cis* –CH=CH–); ^1H NMR: δ 3.73 (3H, *s*, –OMe), 3.93 (3H, *s*, –COOMe), 5.80 and 6.80 (2H, AB *q*, $J = 12$ Hz, *cis* –CH=CH–), 6.91–7.82 (3H, arom. H). The purity of **6** was tested in the same way as **5**. (v) Fatty acid methyl esters and fatty acids. The fatty acid methyl esters were subjected to co-GLC at 190° on DEGS with authentic samples. The fatty acids, after methylation with CH_2N_2, were subjected to co-GLC (190°, DEGS) with authentic samples. The esters and acids found are given in Table 1. (vi) (2*E*)-3-(4-Hydroxy-3-methoxyphenyl) propenic acid (*trans*-ferulic acid) (**7**) ($C_{10}H_{10}O_4$) was isolated by prep. TLC with $CHCl_3$–MeOH–di-isopropyl ether (7 : 3 : 3). Mp 174°; IR ν_{max}^{Nujol} cm^{-1}: 3679–2092 (COOH), 3359 (OH), 1641, 1599, 1546, 1516 (arom. C=C), 975 (*trans* –CH=CH–); ^1H NMR: δ 3.93 (3H, *s*, –OMe), 6.76 and 7.73 (2H, AB *q*, $J = 16$ Hz, *trans* –CH=CH–), 6.31–7.08 (3H, arom. H). This acid (**7**) was identified by direct comparison (mp, mmp, TLC, IR, ^1H NMR and HPLC) with an authentic sample. (vii) (2*Z*)-3-(4-Hydroxy-3-methoxyphenyl) propenic acid (*cis*-ferulic acid) (**8**) ($C_{10}H_{10}O_4$) was confirmed by co-TLC and co-HPLC (on Si ODS with MeOH) with an authentic sample.

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