3-(4-Methyl-3-pentenyl)-2(5H)-furanone, $\alpha,\alpha$-Acariolide and 4-(4-Methyl-3-pentenyl)-2(5H)-furanone, $\alpha,\beta$-Acariolide: New Monoterpenoid Lactones from the Astigmatid Mites, *Schwiebea araujoae* and *Rhizoglyphus* sp. (Astigmata: Acaridae)†

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Received August 6, 2001; Accepted September 25, 2001

A new monoterpenoid lactone from the acarid mite, *Schwiebea araujoae*, was elucidated without its isolation by GC/FT-IR and GC/MS analyses to be 3-(4-methyl-3-pentenyl)-2(5H)-furanone (1) and tentatively named as $\alpha,\alpha$-acariolide. The structure of 1 was identified by its synthesis from $\alpha$-bromo-$\gamma$-butyrolactone via 4 reaction steps. The synthesized compound gave the same GC/MS and GC/FT-IR spectra as those of the natural product.

The other monoterpenoid lactone was likewise elucidated from the unidentified *Rhizoglyphus* mite to be 4-(4-methyl-3-pentenyl)-2(5H)-furanone (2) and named as $\alpha,\beta$-acariolide; it was also identified by its synthesis in 5 reaction steps from the same butyrolactone as the starting material. GC/MS and GC/FT-IR spectra of the preparation were identical to those of the natural product.

Key words: *Schwiebea araujoae*; monoterpenoid lactone; $\alpha,\alpha$-acariolide; 3-(4-methyl-3-pentenyl)-2(5H)-furanone; $\alpha,\beta$-acariolide; 4-(4-methyl-3-pentenyl)-2(5H)-furanone

We are studying the chemical components excreted from the pair of opisthonotal glands commonly present among astigmatid mites for as many species of mites as possible. Parts of these compounds function as semiochemicals (alarm, aggregation and sex pheromones) to each corresponding species. At present, a total of 67 compounds comprising monoterpenes, hydrocarbons and aromatics have so far been identified as the opisthonotal gland components from 52 species of astigmatid mites belonging to 9 families. The alarm pheromones have been identified in 16 species, the aggregation pheromones in two species, and the sex pheromones in seven species. Several compounds also function as anti fungal substances.1,2,3

In the present study, two monoterpenoids were newly found from the acarid mite *Schwiebea araujoae*, and from an unidentified *Rhizoglyphus* sp. other than those already summarized.1) Both species collected from organic soil are possible pests of agricultural crops. In order to elucidate the chemical structures of the remaining unidentified components, their opisthonotal gland secretions were reinvestigated by using a mite extract prepared by dipping mites in hexane for 3 min, and we could identify the structure of the two new monoterpenoids as each isomer based on the mass fragmentation pattern. Both compounds were identified by syntheses.

In the hexane rinse of *Schwiebea araujoae* females, a new compound (I, $t_R$: 12.34 min) was recognized as the second major component after heptadecadiene ($t_R$: 14.88 min) by a GC/MS analysis. The following eight compounds in decreasing order were also observed in the extract: isorobinal4 ($t_R$: 10.99 min), neral5 ($t_R$: 9.48 min), $\alpha$-acaridal5 ($t_R$: 10.06 min), robinal8 ($t_R$: 12.03 min), dehydrocineole8 ($t_R$: 5.62 min), heptadecene ($t_R$: 14.95 min) and isopiperitenone9 ($t_R$: 9.96 min). Compound 1 gave the M+ ion at $m/z$ 166 (31%) and the base ion at $m/z$ 69 (100%) together with a characteristic diagnostic ion at $m/z$ 98 (81%) (Fig. 1). The base ion at $m/z$ 69 suggested the presence of a 4-methyl-3-pentenyl moiety in the molecule. The rearranged fragment ion at $m/z$ 98 implies another part of the molecule, because the sum of $m/z$ 69 and $m/z$ 98 is $m/z$ 166 + $m/z$ 1. The GC/FT-IR spectrum of 1 indicated an unusually high C=O band at 1791 cm$^{-1}$, which is evidence for the presence of a five-membered conjugated lactone moiety (Fig. 2). The putative frag-
ment ion of a lactone with a methylene moiety corresponds to \( m/z 97 \) which actually appeared as the rearranged ion at \( m/z 98 \), as shown in Fig. 3. If compound 1 is assumed to be an intramolecular Canizzaro reaction product of \( \alpha \)-acaridial present in the species, the structure of 1 might be either 3-(4-methyl-3-pentenyl)-2(5H)-furanone or 4-(4-methyl-3-pentenyl)-2(5H)-furanone.

During GC/MS analyses of the extracts from an unidentified *Rhizoglyphus* mite, we found another compound (2, \( t_k: 13.44 \) min) in addition to 1, both as minor compounds as will be indicated later. Compound 2 gave a similar mass spectrum to that of compound 1, but with a different \( t_k \) value. The species was characterized from the other *Rhizoglyphus* species by the presence of eicosadienal\(^6\) (\( t_k: 19.97 \) min, often as the largest component) in the gland secretion, together with the following 16 compounds in decreasing order: tridecane\(^12\) (\( t_k: 10.28 \) min), \( \alpha \)-acaridial\(^8\) (\( t_k: 10.06 \) min), neryl formate\(^13\) (\( t_k: 10.01 \) min), isorobinal\(^9\) (\( t_k: 10.99 \) min), robinal\(^9\) (\( t_k: 12.03 \) min), 3-hydroxybenzene-1,2-dicarbaldehyde\(^14\) (\( t_k: 10.21 \) min), \( \beta \)-acaridial\(^5\) (\( t_k: 11.04 \) min), rhizoglyphinyl formate\(^6\) (\( t_k: 12.43 \) min), eicosenal\(^9\) (\( t_k: 20.14 \) min), geraniol (\( t_k: 9.64 \) min), geranial\(^7\) (\( t_k: 9.90 \) min), 2, 1, nerol (\( t_k: 9.28 \) min), neral\(^7\) (\( t_k: 9.48 \) min) and perillene\(^17\) (\( t_k: 7.37 \) min).

The GC/MS spectrum of 2 showed the same sets of the following ions as those of 1: \( m/z 166 (M^+, 8\%) \), \( m/z 69 \) (the base ion), \( m/z 98 \) (28\%, the rearranged fragment ion), \( m/z 138 \) (11\%), \( m/z 121 \) (8\%) and \( m/z 109 \) (8\%). The relative intensities of the M\(^+\) ion and \( m/z 98 \) are lower than that of 1, whereas those of
confirmed to be identical to those of the natural reported.19) Oxidation of methylthio-(4)-pentenyl)-2(5H)-furanone or 4-(4-methyl-3-pentenyl)-2(5H)-furanone.

The synthetic routes to 1 and 2 are shown in Fig. 4. A mixture of α-bromo-γ-butyrolactone and dimethylsulfide (Me₂S) was refluxed to give α-methylthio-γ-butyrolactone (3, 96%) by following the reported method.20) Butyrolactone 3 was then reacted with 5-iodo-2-methyl-2-pentene dissolved in hexamethylphosphoramide (HMPA) by using lithium disopropylamide (LDA) to give α-(4-methyl-3-pentenyl)-α-methylthio-γ-butyrolactone (4, 57%) as reported.20) Oxidation of 4 by 2KHSO₅/KHSO₃/K₂SO₄ (OXONE) as reported gave α-(4-methyl-3-pentenyl)-α-methylsulfonyl-γ-butyrolactone (5, 50%). Butyrolactone 5 was refluxed in toluene to give target compound 1 (87%). Reduction of 4 with diisobutylaluminum hydride (DIBAL) gave 2-(4-methyl-3-pentenyl)-2-methylthio-1,4-butanediol (6, 96%). Dioil 6 was reacted with OXONE to give 2-(4-methyl-3-pentenyl)-2-methylthiophenol-1,4-butanediol (7, 27%), and subsequent oxidation of 7 with pyridinium dichromate (PDC) gave target compound 2 (30%).

1H-NMR together with 13C-NMR of synthetic 1 demonstrated the presence of a prenyl group; two methyls at δ_H 1.61 (3H, s) and 1.69 (3H, s), a vinyl proton at δ_H 5.10 (1H, br.qn) and two methylene protons at δ_H 2.24–2.33 (4H, m), together with a dimethyl-substituted sp² carbon at δ_C 133.9. All the other protons observed were a vinyl at δ_H 7.15 (1H, qn, J = 1.70 Hz) and an oxygen-substituted methylene at δ_H 4.77 (2H, q, J = 1.70 Hz). These observations suggested that the lactone carbonyl must be endocyclically conjugated with the other double bond in the molecule. The 1H–1H COSY experiment also supported the structure of synthetic 1 (Fig. 5). The GC/MS and GC/FT-IR spectra of synthetic 1 were confirmed to be identical to those of the natural product from Schwiebea araujoae females (Figs. 1 and 2).

The chemical shifts of two methyls [δ_H 1.62 (3H, s) and 1.70 (3H, d, J = 1.40 Hz)], a vinyl [δ_H 5.07 (1H, thp, J = 6.95, 1.40 Hz)] and two methylenes [δ_H 2.29 (2H, dt, J = 7.14, 6.95 Hz) and 2.45 (2H, t, J = 7.14 Hz)] in synthetic 2 indicated the presence of a prenyl group in the molecule, together with a dimethyl-substituted sp² carbon at δ_C 133.8. The other protons observed for synthetic 2 were a vinyl at δ_H 5.84 (1H, qn, J = 1.71 Hz) and an oxygen-substituted methylene at δ_H 4.73 (2H, d, J = 1.71 Hz). The 1H–1H COSY experiment is summarized in Fig. 5. The GC/MS and GC/FT-IR spectra of synthetic 2 were identical to those of the natural product from Rhizoglyphus sp. (Figs. 1 and 2).

A similar monoterpene lactone, (E)-2-(4-methyl-3-pentenylidene)-4-butanolide, has been identified from the mold mite, Tyrophagus putrescentiae, and named as β-acaridial.21) The present identification of 1 and 2 provide the second and third examples of lactones being found among astigmatid mites. In conclusion, 3-(4-methyl-3-pentenyl)-2(5H)-furanone (1) and 4-(4-methyl-3-pentenyl)-2(5H)-furanone (2) were identified as new compounds from the acarid mites, Schwiebea araujoae and Rhizoglyphus sp., respectively. Compound 1 was tentatively named as α,α-acaridial, and 2 as α,β-acaridial, correlating the first double bond to α-acaridial [(E)-2-(4-methyl-3-pentenyl)-butenedial] and the alkenyl substituted position of the lactone ring. Trial exposure of mites to each of synthetic compounds 1 and 2 in stock cultures evoked no remarked effect on either species, so their biological functions remain obscure at present.

Experimental

The astigmatid mite Schwiebea araujoae, was collected from organic soil behind our laboratory at Kyoto University. The other unidentified Rhizoglyphus sp. was collected from Kochinda in Okinawa. Cultures of both species were maintained.
at 20°C under high humidity by feeding dried yeast.

GC/MS was carried out by a Hewlett Packard HP-5890 series II Plus gas chromatograph/mass spectrometer operated at 70 eV in the split-less mode, using an HP-5MS capillary column (0.25 mm ID x 30 m x 0.25 μm in film thickness). The oven temperature was programmed from 60°C (2-min hold) to 290 °C at the rate of 10°C/min, using helium as the carrier gas at 1.20 ml/min. GC/FT-IR spectra were recorded by a Bio-Rad FT-IRD instrument coupled with the foregoing GC apparatus and column under the stated conditions.

1H- and 13C-NMR spectra were obtained by a Bruker AC300 instrument (1H: 300 MHz, 13C: 75 MHz) in CDCl3. 1H–1H COSY analyses were carried out to confirm the structure of the synthetic compounds by a Bruker ARX500 instrument (1H: 500 MHz). All the solvents used for syntheses were dried and freshly distilled. Wako-gel C-200 was used for column chromatography with the indicated solvents. HRMS data were obtained by a Jeol JMS HX/HX 110A spectrometer.

α-Methylthio-γ-butyrolactone (3). A mixture of α-bromo-γ-butyrolactone (25 g, 150 mmol) and Me2S (50 ml, 680 mmol) was refluxed for 40 hrs in an N2 atmosphere. After cooling to r.t., the precipitated trimethylsulphonium bromide was removed by filtration, and the resulting residue was washed with ether. The combined filtrate and washings were concentrated in vacuo to give a pale yellow oil which was purified in a silica gel column. The product (3) as an oil (19.1 g, 96%) was obtained in the fraction eluted with a mixture of hexane and ether. 1H-NMR (300 MHz, CDCl3) δ: 2.10-2.20 (1H, m, ring O–CH2CH2CH2(SMe)–), 2.29 (3H, s, S–CH3), 2.66-2.73 (1H, m, ring O–CH2CH2CH2(SMe)–), 3.44 (1H, dd, J = 9.45, 4.69 Hz, ring CO–CH(SMe)–), 4.33 (1H, ddd, J = 8.95, 8.06, 4.54 Hz, ring O–CH2CH2–), 4.44 (1H, dt, J = 8.95, 7.52 Hz, ring O–CH2CH2–). 13C-NMR (75 MHz, CDCl3) δ: 14.5 (S–CH3), 29.7 (–CH2–), 40.8 (–CH(SMe)–CO), 66.8 (–CH2–O), and 175.2 (CO). GC/MS: M+ at m/z 86 with tR 8.96 min.

α-(4-Methyl-3-pentenyl)-α-methylthio-γ-butyrolactone (4). A solution of 3 (8.0 g, 60 mmol) in THF (20 ml) was slowly added to a mixture of LDA in hexane/THF/ethylbenzene (2 ml, 40 ml) and THF (30 ml) at −78°C while stirring. After 1 hr of stirring, a solution of 5-iodo-2-methyl-2-pentene (12.6 g, 60 mmol) in HMPA (10.7 g, 60 mmol) was slowly added, and the mixture stirred for 3 hrs at −78°C. The temperature was then raised to r.t. while stirring and the mixture kept over night. After adding satd. aq. NH4Cl, the reaction mixture was extracted three times with ether, washed with brine and dried over Na2SO4. After concentration, the crude product was purified in a silica gel column by eluting with a mixture of hexane and ether to give 4 as a colorless oil (7.4 g, 57%). 1H-NMR (300 MHz, CDCl3) δ: 1.63 (3H, s, CH3–C=), 1.68 (1H, m, −CH2CHCH3–), 1.69 (3H, s, CH3–C=), 1.95 (2H, m, −CH2CHCH3–), 2.08 (1H, ddd, J = 13.65, 6.08, 1.34 Hz, O–CH2CH2–), 2.11 (3H, s, CH3–S), 2.26 (1H, m, −CH2CHCH3–), 2.42 (1H, ddd, J = 13.65, 10.83, 8.75 Hz, O–CH2CH2–), 4.34 (1H, dt, J = 8.75, 8.75, 1.34, O–CH2–), 4.43 (1H, ddd, J = 10.83, 8.75, 6.08, O–CH2–) and 5.12 (1H, m, −CH=). 13C-NMR (75 MHz, CDCl3) δ: 11.4 (CH3–S), 17.6 (−CH2–), 22.9 (−CH2–), 25.6 (−CH3), 32.8 (ring, −CH2–), 34.9 (−CH2–), 48.6 (ring, −C–), 65.1 (ring, O–CH2–), 122.8 (CH=), 132.7 (C=) and 175.4 (CO). GC/MS: M+ at m/z 214 (21%) and the base ion at m/z 132 with GC tR 14.88 min.

α-(4-Methyl-3-pentenyl)-α-methylsulfonyl-γ-butyrolactone (5). A solution of OXONE, (1.4 g, 2.3 mmol) in water (30 ml) was added to a mixture of methanol (15 ml) and 4 (500 mg, 2.3 mmol) at 0°C, and the resulting cloudy slurry was kept for 6 hrs while stirring. After the temperature has been raised to r.t. while stirring and the mixture kept over night, the product was extracted three times with ether. The combined organic layers were successively washed with satd. NaHCO3 and brine, and dried over Na2SO4. Oily yellowish product 5 (290 mg, 50%) was obtained after concentrating the extract. 1H-NMR (300 MHz, CDCl3) δ: 1.62 (3H, s, CH3–C=), 1.70 (3H, s, CH3–C=), 2.08 (4H, m, −CH2CHCH3–), 2.52 (1H, dt, J = 14.84, 8.70 Hz, O–CH2CH2–), 3.04 (1H, ddd, J = 14.84, 8.70, 3.51 Hz, O–CH2CH2–), 3.09 (3H, s, CH3–S), 4.36 (1H, dt, J = 8.70, 3.51, O–CH2–), 4.51 (1H, q, J = 8.70, O–CH2–) and 5.06 (1H, br.t, −CH=). 13C-NMR (75 MHz, CDCl3) δ: 17.6 (−CH3), 22.9 (ring −CH2–), 25.1 (−CH3), 25.6 (CH3–S), 32.1 (−CH2–), 36.0 (−CH2–), 66.5 (O–CH2–), 70.6 (ring C), 121.1 (−CH=), 134.4 (C=) and 172.8 (CO). GC tR: 16.97 min. GC/MS: M+ at m/z 246 (8%) and the base ion at m/z 82.

α,α-Acariolide (1). A toluene (60 ml) solution of 5 (290 mg) was refluxed for 7 hrs. After purification in a silica gel column eluted with a mixture of hexane and ether, the target compound (1, 170 mg, 87%) was obtained as a colorless oil. 1H-NMR (300 MHz, CDCl3) δ: 1.61 (3H, s, =C–CH3), 1.69 (3H, s, =C–CH3), 2.24-2.33 (4H, m, =CH2CH2CH2–), 4.77 (2H, q, J = 1.70 Hz, −CH2O–), 5.10 (1H, br, qn, −CH2CH=CH2CMe3) and 7.15 (1H, qn, J = 1.70 Hz, O–CH2CH=CH2–). 13C-NMR (75 MHz, CDCl3) δ: 17.7 (−CH3), 25.4 (−CH2–), 25.6 (−CH3), 25.7 (−CH2–), 70.1 (O–CH2–), 122.7 (−CH=), 133.0 (C=), 133.9 (ring C=), 144.3 (ring −CH=) and 174.4 (CO). GC/MS: M+ at m/z 166 (17%) and the base ion at m/z 69 together with m/z 98 (82%) and m/z 41 (54%). GC
2-(Methyl-3-pentenyl)-2-methylthio-1,4-butanediol (6). To a solution of α-(4-methyl-3-pentenyl)-α-methylthio-γ-butyrolactone (4, 1.07 g, 5 mmol) in ether (10 ml), DIBAL (2 ml, 11 mmol) was slowly added at 0°C and the mixture stirred for 1 hr at r.t. After adding satd. aq. NH₄Cl (10 ml) at 0°C, the product was obtained as the filtrate through Celite, and dried over Na₂SO₄. After evaporating the solvent, the crude product was chromatographed on silica gel, eluting with hexane and ether to give 6 as a colorless oil (1.04 g, 95%). ¹H-NMR (300 MHz, CDCl₃) δ: 1.46–1.59 (2H, m, C–CH₂CH₂CH₃ =), 1.62 (3H, s, CH₃), 1.69 (3H, s, CH₃C=), 1.76–1.89 (2H, m, C–CH₂CH₂O =), 1.95 (3H, s, CH₃–S), 2.02–2.17 (2H, m, C–CH₂CH₂CH₂ =), 3.01 (2H, br s, –OH), 3.52 (2H, s, –C=CH₂O =), 3.70–3.78 (1H, m, C–CH₂CH₂O =), 3.83–3.91 (1H, m, C–CH₂CH₂O =) and 5.08–5.12 (1H, m, –CH₂CH = C(Me)₂). ¹³C-NMR (75 MHz, CDCl₃) δ: 9.6 (S–CH₃), 17.7 (–CH₂–), 22.1 (–CH₂–), 25.7 (–CH₂–), 33.8 (–CH₂–), 37.4 (–CH₂–), 52.5 (C), 58.7 (O–CH₂–), 65.5 (O–CH₂–), 123.7 (=CH) and 132.2 (=C). GC/MS: M⁺ at m/z 218 (9%) and the base ion at m/z 69 together with m/z 152 (36%), 140 (13%), 121 (44%), 107 (29%), 95 (48%), 82 (63%), 55 (30%), and m/z 41 (67%). GC tᵣ: 13.44 min. HRMS m/z (M⁺): calcld. for C₁₀H₁₄O₂, 166.0994; found, 166.0999.

2-(Methyl-3-pentenyl)-2-methylsulfonyl-1,4-butanediol (7). To a methanolic (20 ml) solution of 6 (940 mg, 4.3 mmol), a solution of OXONE (2.6 g, 4.3 mmol) in water (20 ml) was added at 0°C. The resulting cloudy slurry was kept for 2 hrs at 0°C while stirring. After filtration, the filtrate was concentrated in vacuo, and the product was extracted four times with ether. The combined organic layer was successively washed with satd. aq. NaHCO₃ and brine, and dried over Na₂SO₄. After being concentrated, the crude product was chromatographed in a silica gel column, and the product was eluted with ether. After evaporating the solvent, the crude product was further purified in a silica gel column, and the product was eluted with ethylacetate and benzene to give 7 (30%) as a colorless oil. ¹H-NMR (300 MHz, CDCl₃) δ: 1.62 (3H, s, CH₃C=), 1.70 (3H, d, J = 1.40 Hz, CH₃C=), 2.29 (2H, d, J = 1.74 Hz = CH–CH₂CH₂C=), 2.45 (2H, t, J = 1.74 Hz = CH–CH₂CH₂C=), 4.73 (2H, d, J = 1.71 Hz = C–CH₂–O), 5.07 (1H, tq, J = 6.95, 1.40 Hz, –CH₂CH = C(Me)₂) and 5.84 (1H, qn, J = 1.71 Hz, –C(O)–CH =). ¹³C-NMR (75 MHz, CDCl₃) δ: 17.7 (=CH₂–), 25.6 (=CH₂–), 25.7 (=CH₂–), 28.6 (=CH₂–), 73.1 (=O–CH₂–), 115.5 (=C(O)–CH =), 121.9 (CH =), 133.8 (=C =), 170.2 (ring C =) and 174.1 (CO). GC tᵣ: 13.44 min. HRMS m/z (M⁺): calcld. for C₁₀H₁₄O₂, 166.0994; found, 166.0998.

Acknowledgments

This study was partly supported by a grant-aid for scientific research from Ministry of Education, Science, Sports and Culture of Japan (nos. 08406010, 09556010, 09876091 and 8956), and also by research funding from Daily Foods Corporation (Tokyo). We thank Dr. N. Akimoto of Faculty of Pharmaceutical Sciences at Kyoto University for measuring the HRMS data.

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