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FURTHER ALKYL AND ALKENYLPHENOLS OF *KNEMA LAURINA* AND *KNEMA AUSTROSIAMENSIS*: LOCATION OF THE DOUBLE BOND IN THE ALKENYL SIDE CHAINS

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Key Word Index—*Knema austrosiamensis*; *Knema laurina*; Myristaceae; cardanols; anacardic acids; acylresorcinols; acylphloroglucinols.

Abstract—Further work on the constituents of *Knema laurina* stem bark and *K. austrosiamenis* wood furnished one new cardanol, two new anacardic acids, two new acylresorcinols, one new acylphloroglucinol and 7-hydroxy-3,′4′-methylenedioxyflavan. Locations of the double bonds in the side chains of these and previously reported constituents were established by means of methylthiomethylation-GC–mass spectrometry. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

In previous articles we reported, *inter alia*, the isolation of compounds **1a** and **2a** from the stem bark of *Knema laurina* Warb [1] and compounds **4a**, **b**, **d**, **e** and **5a**, **b** from wood of *K. austrosiamensis* W. J. J. O. De Wilde [2]. In the case of compounds **5a**, **b** the location of the side chain double bond was not specified although the sum of m + n was shown to be 5. Further study of a fraction of the *K. laurina* extract has now led to isolation of the new compounds **1b**, **2b** and **3**, and also 7-hydroxy-3′4′-methylenedioxyflavan [3], while some fractions of the *K. austrosiamensis* extract have furnished, in addition, the new compounds **4c** and **4f**. Methylthiomethylation-GC–mass spectrometry [4, 5] confirmed the previously deduced [1] location of the double bond in compound **1a** and established the locus of the double bonds in compounds **1b**, **3**, **5a** and **5b**.

RESULTS AND DISCUSSION

We deal first with the saturated derivatives **2b**, **4c** and **4f**. Mass spectrometry, ^{1}H and ^{13}CNMR spectra (see Experimental) clearly showed that compound **2b**, was a lower homologue, $n = 10$, of the previously encountered compound **2a** from *K. laurina* [1], while compounds **4c** and **4f** were likewise $n = 10$ analogues of resorcinols compounds **4a** and **4b**, resp. phloroglucinol derivatives **4d** and **4e** from *K. austrosiamensis* [2]. In addition to the molecular ions $[M]^+$ mass spectra of compounds **4c** and **4f** exhibited significant peaks at *m/z* 152 and 168, respectively, characteristic of the McLafferty rearrangement.

MS, ^{1}H and ^{13}C NMR spectra of compound **1b** and the properties of the corresponding diacetate (see Experimental) showed that it was the resorcinol analogue of phenol **1a** obtained previously from *K. laurina* [1]. To locate the double bond in the chain linking the two rings we used a procedure involving addition of dimethyldisulfide to the double bond followed by GC–mass spectrometric analysis [4, 5]. As illustrated (Scheme 1) for compound **1a**, for which we earlier inferred location of the double bond from analysis of the ^{1}H and ^{13}C NMR spectra, the adducts cleave preferentially across the C–C bond between the CH_3S– substituents, leading to two major fragment ions A^+ and B^+ which define location of the double bond and may fragment further as shown. In the case of resorcinol derivatives, such as compound **1b**, aromatic substitution *para* to the side chain by the CH_3S– group accompanies addition to the double bond.

As shown in Scheme 2 application of the method to compounds **5a** and **5b** isolated earlier from *K. austrosiamensis* located the double bond at carbon atoms 8′ and 9′ away from the carbonyl group, i.e. $m = 4$ and $n = 1$. Finally, the fragments from anacardic acid (**3**), which underwent decarboxylation at the temperature used for dithiomethylation (Scheme 3), located the double bond again at C-8′ of the side chain.

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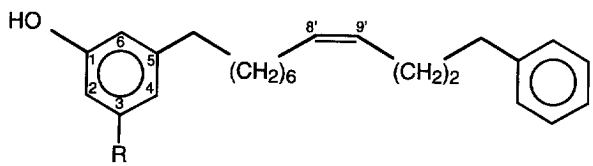
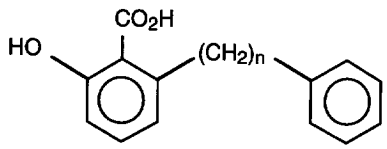
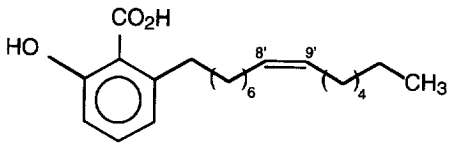


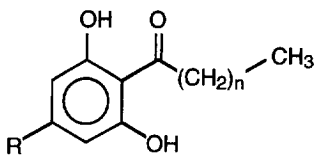
1 a R = H
b R = OH



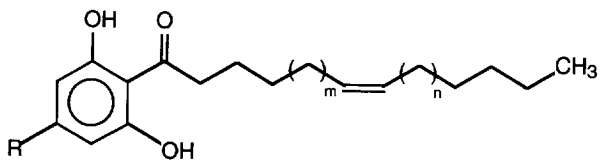
2 a n = 12
b n = 10



3



4 a R = H, n = 8
b R = H, n = 12
c R = H, n = 10
d R = OH, n = 8
e R = OH, n = 12
f R = OH, n = 10



5 a R = H, m=4, n=1
b R = OH, m=4, n=1

EXPERIMENTAL

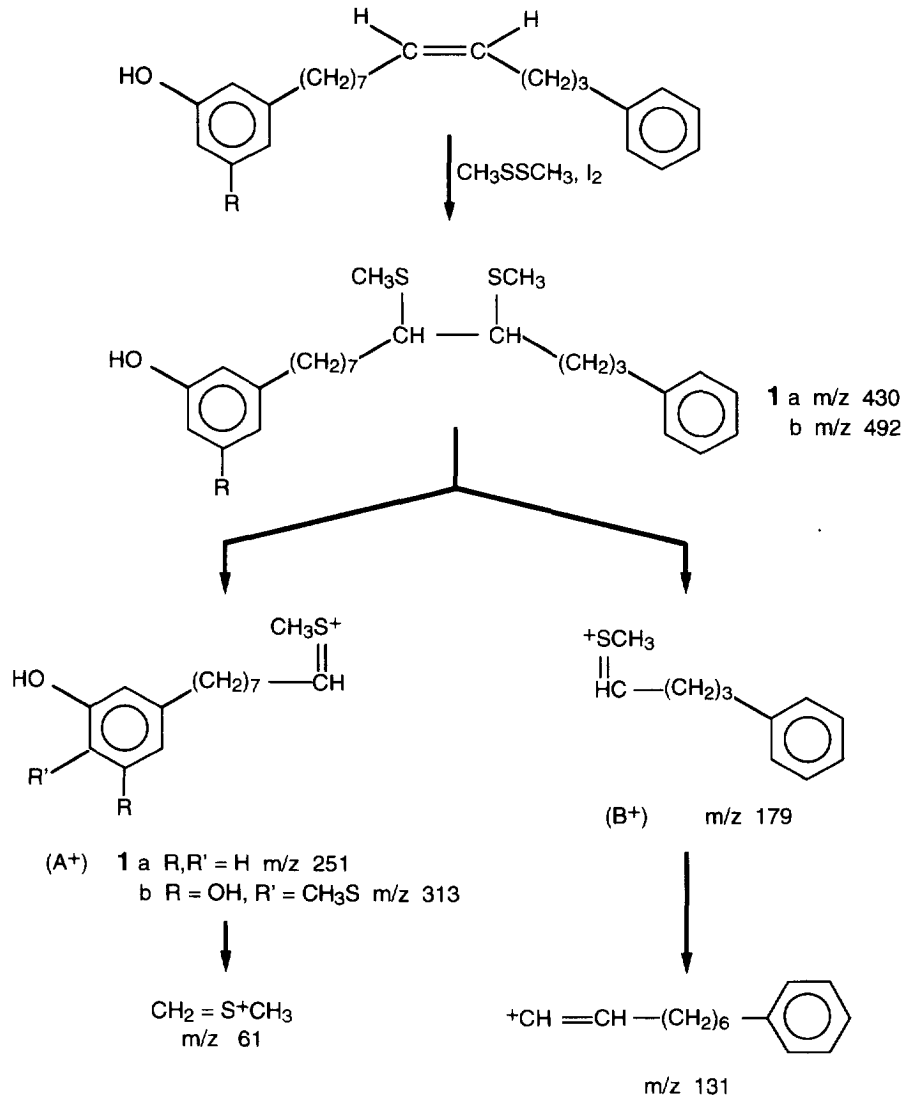
Isolation of new constituents. (A) Frs 58–70 (512 mg) of the original chromatogram of the *K. laurina* extract [1] were combined and rechromatographed over Si gel, 20 ml subfractions being collected as follows: Subfrs. 1–20 (petrol–$CHCl_3$, 4:1), 21–40 (petrol–$CHCl_3$, 7:3), 42–60 (petrol–$CHCl_3$, 1:1), 61–70 (petrol–$CHCl_3$, 3:7). Subfrs. 42–70 (280 mg) were combined and purified by PTLC (Si gel, $CHCl_3$–acetone, 4:1) to give 7-hydroxy-3′,4′-methylenedioxyflavan, yellow crystals, mp 123–125°, identified by IR, UV, ^1H and ^{13}C NMR and conversion to the acetate, ^1H and ^{13}C as reported in ref. [3]. Frs 79–95 (950 mg) of the original chromatogram were combined and rechromatographed over Si gel, 20-ml subfrs being collected as follows: Subfrs 1–14 (petrol–$CHCl_3$, 4:1), 15–67 (petrol–$CHCl_3$, 1:1) and 68–89 (petrol–$CHCl_3$, 1:4). Subfrs 11–14 (65 mg) were combined and purified by PTLC (Si gel, $CHCl_3$) to give compound **1a** (25 mg), as described in ref. [1]. Subfrs 68–89 (90 mg) were combined; PTLC (Si gel, $CHCl_3$–Me_2CO, 4:1) yielded 45 mg of compound **1b**. Combination of subfrs 96–124 (500 mg) and reverse-phase HPTLC (stationary phase RP-18 F254S, mobile phase (CH_3CN) yielded compounds **2b** (30 mg), **2g** [1] (22 mg), and **3** (20 mg).

(B) GC–MS analysis of frs 52–56 of the *K. austrosiamensis* chromatogram [2] indicated the presence of four constituents of 292, 318, 320 and 326 amu, respectively. Sepn by reverse-phase HPTLC (RP-18 F2545, CH_3CN) gave compounds **5a** [2], **4b** [2], **4a** [2] and **4c** (4 mg). GC–mass spectral of frs 162–186 showed the presence of four constituents 308, 334, 336 and 342 amu, respectively. Sepn by reverse-phase HPTLC gave compounds **5b** [2], **5c** [2] **4c** [2] and **4f** (7 mg).

The procedure for thiomethylation mass spectrometry was that of ref. [5] with the slight modification that the reaction mixt. was kept overnight at 100°. Aliquot GC–MS analyses were carried out using an Hewlett-Packard HP 5890A instrument equipped with selective mass detector model MSD 5970, a control system and data work station HP 59970. The column employed was a capillary column DB-Wax (30 m × 0.25 mm i.d., J & W). Carrier gas was helium N60 with a flow rate of 0.9 ml min^{-1} at 150°. The temperature of the injector and interphase area was 300°. Samples were injected in the splitless mode (1 μ) with 2 min of purge off time. The column temp. was programmed at 100° for 2 min and from 100–250° at the rate of 2°/min, then from 250 to 300° at the rate of 2°/min and maintained at 300°. The mass spectrometer was operated from 50 to 530 amu with full-scan detection.

3-(12-*Phenyl*-8Z-*dodecenyl*)*phenol* (**1a**). [1] EI-MS of the dithiomethylated adduct *m/z* (rel. int.): 430 $[M]^+$, $C_{26}H_{38}O_2$ (40), 251 (48), 179 (10), 131 (100), 107 (4), 91 (30), 61 (18).

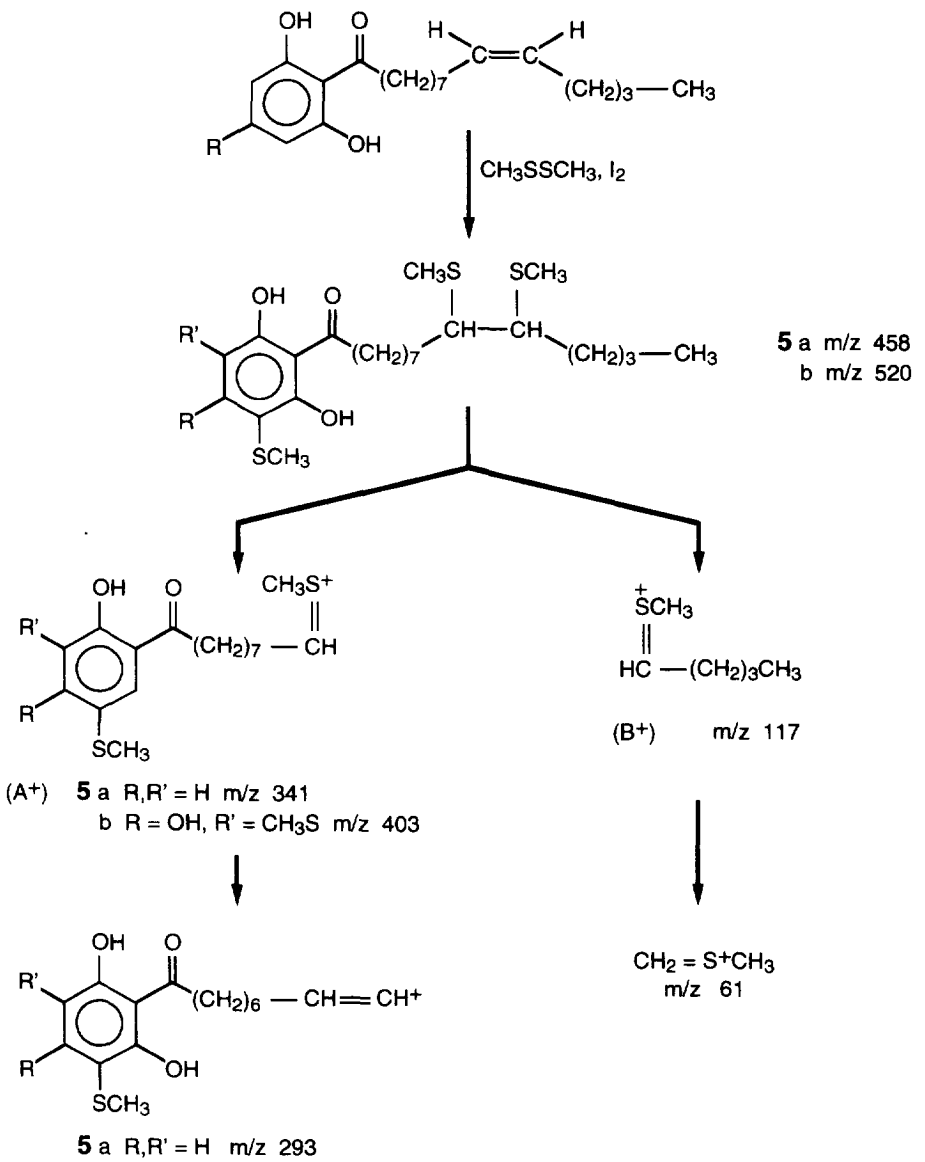
5-(12-*Phenyl*-8Z-*dodecenyl*)-*resorcinol* (**1b**). Gum, EI-MS *m/z* (rel. int.): 352 $[M]^+$, $C_{24}H_{32}O_2$, (3), 326 (4), 318 (8), 292 (3), 205 (4), 191 (4), 177 (3), 166 (6), 165 (3), 149 (4), 138 (3), 137 (14), 125 (8), 124 (100), 123 (42); IR ν_{max}^{KBr}, cm^{-1}: 3600–3200 (OH), 2930, 2860, 1600, 1460, 1450, 1380, 1160, 990, 830; UV λ_{max}^{MeOH} nm (log ε): 210 (3.7), 275 (2.7), 281 (2.7), UV $\lambda_{max}^{MeOH+NaOH}$ nm (log ε): 210 (3.7), 275 (2.7), 281 (2.7); UV $\lambda_{max}^{MeOH+NaOH}$ nm (log ε): 216 (3.9), 289



Scheme 1. Methylthiolation-fragmentation fo compounds **1a** (R=H) and **1b** (R=OH).

(2.9); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.28–7.16 (*m*, 5p, H-2″-H-6″), 6.24 (*br s*, 3p, H-2, 4, 6), 5.60 (*br s*, -OH), 5.36 (centre of AB system of H-8′ and H-9′, $J_{8',9'} \approx 11$ H2, $J_{7',8'} = J_{9',10'} \approx 5$ Hz), 2.61 (*t*, $J=7.5$ Hz, 2p, H-1′), 2.45 (*t*, $J=7.5$ Hz, 2p, H-12′), 2.02 (*m*, 4p, H-7′, 10′), 1.63 (*m*, 4p, H-2′, 11′), 1.27, 1.25 *br s*, 8p, H-3′-H-6′); ^{13}C NMR ($CDCl_3$, 50.3 MHz): 156.5*s* C-1, C-3), 142.9*s*, 142.6*s* (C-5, C-1″), 129.8*d*, 129.3*d* (C-8′, C-9′) 128.4*d* (C-2″, C-6″), 128*d* (C-3″, C-5″), 125.6*d* (C-4″), 108.0*d* (C-4, C-6) 100.2*d* (C-2), 35.8*t* (C-1′), 35.4*t* (C-12′), 31.8*t* (C-2′), 31.5*t* (C-11), 29.2*t*, 28.9*t*, (C-3′ to C-6′), 27.2*t*, 22.6*t*, (C-7′, C-10′). Reaction of compound **1b** (7 mg) with Ac_2O-Py in the usual way followed by purification by TLC (silica gel, petrol–$CHCl_3$, 4:1) gave 5 mg of the diacetate; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.28–7.16 (*m*, 5p, H-2″ to H-6″), 6.80 (*d*, $J=2$ Hz, 2p, H-4, H-6) 6.73 (*t*, $J=2$ Hz, H-2), 5.36 (2p, centre of AB system H-8′ and H-9′, $J_{8',9'} \approx 5$ Hz), 2.59 (*t*, $J=7.5$ Hz, 4p, H-1′, 12′), 2.28 (*br s*, 6p, Ac), 2.01 (*m*, 4p, H-7′, 10′), 1.63 (*m*, 4p, H-2′, 11′), 1.29, 1.25 (*br s*, 8p, H-3′-H-6′); EI-MS of the dithiomethylated adduct of compound **1b** *m/z* (rel. int.): 492 $[M]^+$, $C_{27}H_{40}O_2S_3$, (16), 398 (12), 314 (24), 313 (61), 281 (9), 265 (7), 264 (8), 209 (12), 179 (20), 170 (62), 169 (45), 132 (15), 131 (100), 123 (11), 91 (31), 61 (16), 55 (6).

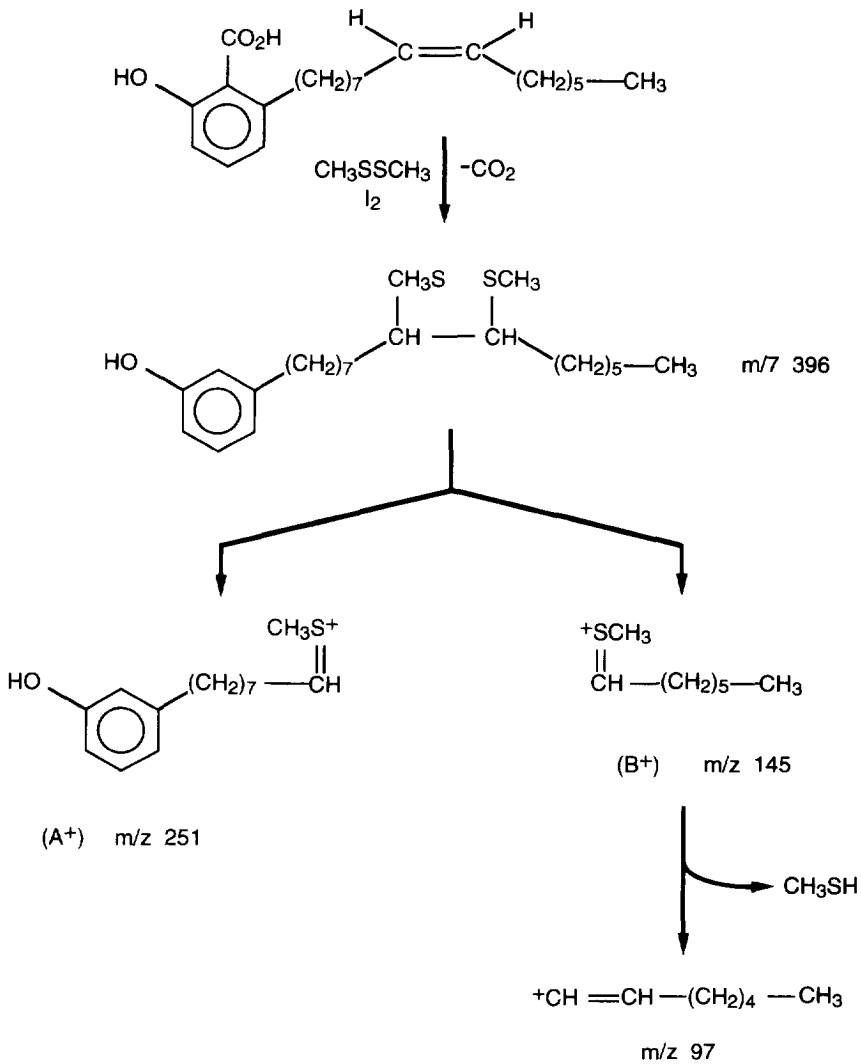
2-*Hydroxy*-6-(10-*phenyldecyl*)-*benzoic acid* (**2b**). Crystalline solid, mp 84–86°C; EI-MS *m/z* (rel. int.): 354 $[M]^+$, $C_{23}H_{30}O_3$, (42), 344 (11), 336 (30), 318 (12), 227 (11), 185 (11), 161 (24), 152 (19), 151 (11), 148 (12), 147 (16), 145 (13), 134 (22), 133 (17), 131 (17), 108 (17), 107 (25), 105 (33), 104 (8), 103 (15), 91 (100); IR ν_{max}^{KBr}, cm^{-1}: 3600–3400, 2920, 2850, 1650, 1600, 1580, 1490, 1450, 1310, 1250, 1210, 900, 810; UV λ_{max}^{MeOH} nm (log ε): 217 (4.2), 242 (3.6), 288 (3.1), 308 (3.4); UV $\lambda_{max}^{MeOH+NaOH}$ nm (log ε: 216 (4.2), 244 (3.6), 298 (3.5); UV $\lambda_{max}^{MeOH+AlCl_3}$; nm (log ε): 21 ′ (4.2), 289 (3.1), 315 (3.3); ^{1}H NMR ($CDCl_3$, 200



Scheme 2. Methylthiolation-fragmentation of compounds **5a** (R = H) and **5b** (R = OH).

MHz): δ 7.35 (*t*, J = 8 Hz, H-4), 7.26–7.14 (*m*, 5p, H-2″-H-6″), 6.86 (*d*, J = 8 Hz, H-3), 6.76 (*d*, J = 8 Hz, H-5), 2.97 (*t*, J = 7 Hz, 2p, H-1′), 2.59 (*t*, J = 7 Hz, 2p, H-10′), 1.63 (*m*, 4p, H-2′, 9′), 1.28, 1.25 *br s* (12p, H-3′-H-8′), ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 175.5*s* (CO_2H), 163.6*s* (C-2), 147.6*s* (C-6), 142.9*s* (C-1″), 135.3*d* (C-4), 1284*d* (C-3″, C-5″), 128.2*d* (C-2″, C-6″), 125.5*d* (C-4″), 122.7*d* (C-5), 115.8*d* (C-3), 110.5*s* (C-1), 36.5*t* (C-1′), 36.5*t* (C-1′), 36.0*t*, 31.5*t* (C-2′, C-9′), 29.7*t*, 29.6*t* (C-3′ to C-8′).

2-Hydroxy-6-(8Z-pentadecenyl)-benzoic acid (**3**). Gum: EI-MS *m/z* (rel. int.): 346 $[M]^+$, $C_{22}H_{34}O_3$, (55), 328 (29), 320 (15), 310 (22), 302 (34), 285 (10), 257 (10), 227 (11), 175 (20), 161 (24), 152 (50), 147 (42), 134 (37), 120 (10), 108 (50), 91 (100); IR ν_{max}^{Kbr}, cm^{-1}: 3600–3200, 2920, 2860, 1650, 1600, 1580, 1450, 125, 1210, 1160, 1120; UV λ_{max}^{MeOH} nm (log ε): 206 (4.7), 303 (3.7); UV $\lambda_{max}^{MeOH+NaOH}$ nm (log ε: 212 (4.9), 297 (3.9); UV $\lambda_{max}^{MeOH+AlCl_3}$; nm (log ε): 303 (4.7), 312 (3.5); ^{1}H NMR (200 MHz $CDCl_3$): δ 7.06 (*t*, J = 8 Hz, H-4), 6.87 (*dd*, J = 8, 1 Hz, H-3), 6.75 (*dd*, J = 8, 1 Hz, H-5), 5.35 (centre of AB system of H-8′ and H-9′, $J_{8',9'} \approx 9$ Hz, $J_{7',8'} = J_{9',10'} \approx 5$ Hz), 2.98 (*t*, J = 7.5 Hz, 2p, H-1′, 2.01 (*m*, 4p, H-7′, 10′, 1.60 (*m*, 2p, H-2′), 1.27 (*br s*, 16p, H-3′ to H-6′, H-11′ to H-14′), 0.87 (*t*, J = 7.5 Hz, 3p, H-15′); ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 175.4*s* (CO_2 H), 163.6*s* (C-2), 147.6*s* (C-6, C-1″), 135.3*d* (C-4), 129.8*d* (C-8′, C-9′), 122.7*d* (C-5), 115.8*d* (C-3), 110.5*s* (C-1), 36.5*t* (C-1′), 32.0*t* (C-2′), 31.8*t* (C-13′), 30.9*t*, 29.7*t*, 28.99*t* (CH_2), 27.2*d* (C-7′ to C-10′), 22.7*t* (C-14′), 14.1*q* (C-15′); EI-MS of dithiomethylated adduct (loss of CO_2) *m/z* (rel. int.): 396 $[M]^+$, $C_{23}H_{40}OS_2$, (22), 252 (19), 251 (100), 203 (6), 147 (27), 145 (50), 144 (13), 133 (19), 120 (9),



Scheme 3. Methylthiolation-fragmentation of compound **3**.

108 (21), 107 (50), 97 (13), 61 (32), 55 (30).

1-(2,6-*Dihydroxyphenyl*)-*dodecan*-1-*one* (**4c**). Gum; EI-MS *m/z* (rel. int.): 292 $[M]^+$, $C_{18}H_{28}O_3$, (12), 274 (10), 189 (15), 176 (10), 152 (30), 137 (100); ^1H NMR $CDCl_3$, 200 MHz): δ 9.68 (*br s*, -OH), 7.17 (*t*, $J=8$ Hz, H-4), 6.36 (*d*, $J=8$ Hz, 2p, H-3, 5), 3.10 (*t*, $J=7$ Hz, 2p, H-2′), 1.68 (*m*, 2p, H-3′), 1.23 (*m*, 16 p, H-4′ to H-11′), 0.85 (*t*, $J=7$ Hz, 3p, H-12′).

1-(2,4,6-*Trihydroxyphenyl*)-*dodecan*-1-*one* (**4f**). Gum; EI-MS *m/z* (rel. int.): 308 $[M]^+$, $C_{18}H_{28}O_4$, (10), 290 (12), 205 (5), 192 (5), 168 (40), 153 (100), 139 (5); ^1H NMR ($CDCl_3$, 200 MHz): δ 5.85 *br s*, 2p, H-3, 5), 3.00 (*t*, $J=6.5$ Hz, 2p, H-2′), 1.5 (*m*, 2p, H-3′), 1.23 (*m*, 16p, H-4′-H-11′), 0.85 (*t*, $J=6.5$ Hz, 3p, H-12′).

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