Identification and Total Synthesis of a Novel Dimethylated Fatty Acid from the Caribbean Sponge *Calyx podatypa*

Néstor M. Carballeira* and Mayra Pagán

Department of Chemistry, University of Puerto Rico, P.O. Box 23346, San Juan, Puerto Rico 00931

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The dimethylated fatty acid 9,13-dimethyltetradecanoic acid was identified for the first time in nature in the Caribbean sponge *Calyx podatypa* where it occurs together with the rare 10,13-dimethyltetradecanoic acid. The characterization of the novel compound was accomplished using GC−MS, pyrrolidide derivatization, and a five-step total synthesis starting with 8-bromooctanoic acid. The first racemic total synthesis for the rare 10,13-dimethyltetradecanoic acid is also described.

Marine fatty acids are of interest for the different roles and biological properties they exhibit in the cells of marine organisms.[1] Some of these fatty acids have displayed interesting biological activities. For example, short-chain fatty acids containing 12−16 carbons, mainly of bacterial origin, display antimicrobial activity against Gram-positive bacteria.[2] On the other hand, longer-chain analogues possessing 26−28 carbons, with the $\Delta^{5,9}$ diunsaturation, are effective as topoisomerase I inhibitors.[3] Just recently, we explored the phospholipid fatty acid composition of the Caribbean sponge *Calyx podatypa* Van Soest (Phloeodictyidae) and found several novel short-chain fatty acids in the complex mixture of more than 85 different fatty acids that were characterized.[4] However, at that time we were unable to characterize two dimethylated fatty acids due to their low abundance and close gas chromatographic coelution of their methyl esters in nonpolar capillary gas chromatography. Several plausible structural candidates for these fatty acids can be proposed guided by our preliminary mass spectral data and biosynthetic considerations. However, the only way left to characterize these compounds was through their total synthesis followed by gas chromatographic coelution of the corresponding natural and synthetic fatty acid methyl esters. We now wish to report the identification and total synthesis of these two acids as the novel 9,13-dimethyltetradecanoic acid and the rare 10,13-dimethyltetradecanoic acid.[5] These acids are of interest because they have the potential to display antimicrobial activity, inasmuch as the monomethylated analogues 13-methyltetradecanoic acid and 12-methyltetradecanoic acid show antimicrobial activity (MIC = 3.13 μg/mL) against *Streptococcus mutans* MT509.[6] Herein we report the results of our investigation.

The fatty acid composition of *C. podatypa* was previously reported, and 85 different saturated, methylated, and polyunsaturated fatty acids were identified.[4] In addition, two dimethylated hexadecanoic acids were not characterized due to their low abundance and almost identical capillary GC elution times (ECL (equivalent-chain length) values of 15.28 and 15.30). Mass spectrometry of their pyrrolidide derivatives suggested, although vaguely, that these compounds could be the unknown 9,13-dimethyltetradecanoic acid and the rare 10,13-dimethyltetradecanoic acid.[5] For example, the mass spectrum of *N*-9,13-dimethyltetradecanoylpyrrolidine displayed a molecular ion peak at *m*/*z* 309 and two key fragmentations, one with a diminished peak at *m*/*z* 280 with higher than normal flanking peaks at *m*/*z* 266 and *m*/*z* 294, and a second diminished peak at *m*/*z* 210 with higher than normal flanking peaks at *m*/*z* 196 and *m*/*z* 224. This suggested methyl branching at carbons 9 and 13.[5] The mass spectrum of *N*-10,13-dimethyltetradecanoylpyrrolidine displayed similar fragmentations, as had been reported earlier.[5]

Final structural confirmation for these dimethylated fatty acids was achieved through their total synthesis. The best route for the racemic synthesis of methyl 9,13-dimethyltetradecanoate (**1**) was achieved through the coupling reaction of 6-methyl-2-heptanone and (7-methoxycarbonylheptyl)triphenylphosphonium bromide (Scheme 1). The known 6-methyl-2-heptanone[7] was obtained in a 91% yield through the catalytic hydrogenation of 6-methyl-5-hepten-2-one. The salt (7-methoxycarbonylheptyl)triphenylphosphonium bromide was readily obtained from commercially available 8-bromooctanoic acid, via esterification with HCl/MeOH followed by reaction with triphenylphosphine.[8] Coupling of the methylated heptanone with the Wittig salt resulted in a 73% yield of a 1.4:1 mixture of the (*Z*/*E*)-isomers of methyl 9,13-dimethyl-8-tetradecenoate, which upon catalytic hydrogenation afforded the desired methyl 9,13-dimethyltetradecanoate (**1**). A GC coelution experiment with the natural methyl esters demonstrated that the first peak of the two closely related GC peaks (ECL = 15.28) indeed corresponded to **1**.

To confirm the structure of the other isomer the racemic synthesis of methyl 10,13-dimethyltetradecanoate (**2**) was also undertaken, which is the first reported synthesis for this compound (Scheme 2). Our synthesis started with commercially available 9-bromo-1-nonanol (Aldrich), which, upon reaction with triphenylphosphine, resulted in a 71% isolated yield of (9-hydroxynonyl)triphenylphosphonium bromide. Reaction of the latter Wittig salt with 5-methyl-2-hexanone, in the presence of potassium *t*-butoxide in THF, resulted in a 69% yield of a 1:1 mixture of the *Z*/*E* isomers of 10,13-dimethyl-9-tetradecen-1-ol. In this reaction some minor hydrocarbon products, such as different *Z*/*E* combinations of 2,5,15,18-tetramethyl-5,4-nonadiene, were also obtained in trace amounts. These hydrocarbon products could have been formed from a nonane-1,9-bis(triphenylphosphonium bromide) salt, which was apparently also formed during the preparation of the phosphonium salt. However, these hydrocarbons were easily removed from the alcohol by Si gel column chromatography. Catalytic hydrogenation of the dimethylated 9-tetradecenol afforded, in quantitative yield, 10,13-dimethyltetradecan-

* To whom correspondence should be addressed. Tel.: (787) 764-0000, ext. 4791. Fax: (787) 756-8242. E-mail: ncarball@upracd.upr.clu.edu.

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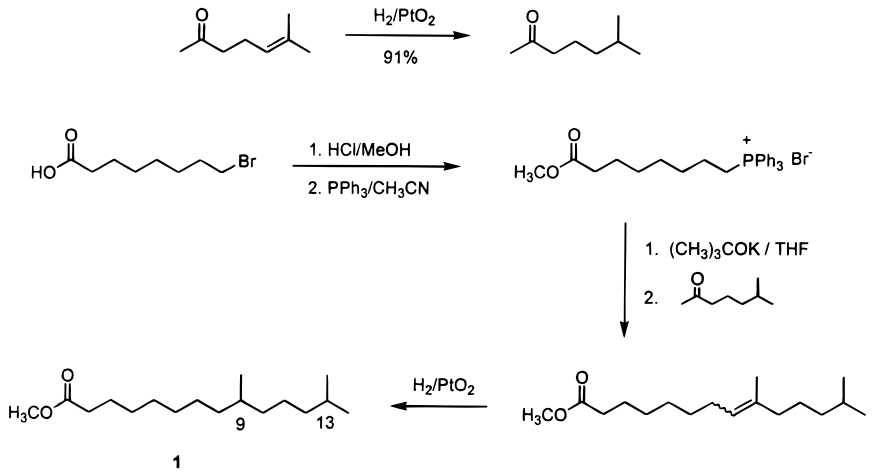
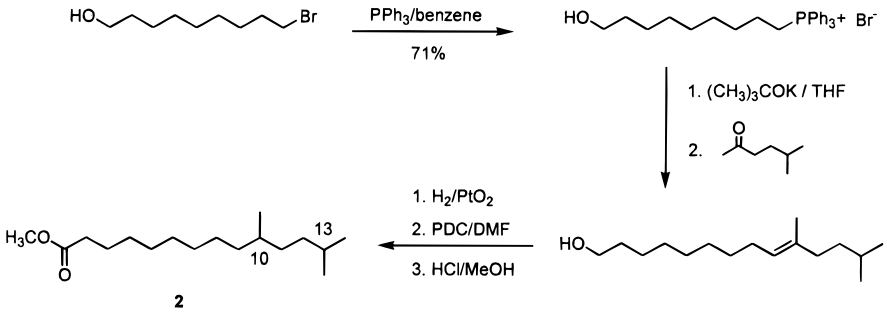
Scheme 1



Scheme 2



1-ol. Interesting to mention at this point is that the related trimethylated alcohol, namely the 6,10,13-trimethyltetradecan-1-ol, is the aggregation pheromone of the predatory stink bug *Stiretrus anchorago*.[9,10] The 10,13-dimethyltetradecan-1-ol was further oxidized with pyridinium dichromate in DMF to the expected 10,13-dimethyltetradecanoic acid, but only trace amounts of the product were isolated. Final esterification in methanolic HCl afforded enough methyl 10,13-dimethyltetradecanoate (**2**) to secure the structure of the natural compound by GC coelution (ECL = 15.30) with the natural methyl esters from *C. podatypa*. We have reported this dimethylated fatty acid earlier from the sponge *Ectyoplasia ferox* based on GC and MS data alone.[5]

We presented here the identification and racemic synthesis of the methyl ester of a new dimethylated fatty acid, namely the 9,13-dimethyltetradecanoic acid. We have also accomplished the first synthesis of the methyl ester of the 10,13-dimethyltetradecanoic acid, a compound first identified in the sponge *E. ferox*.[5] The elution order of the methyl esters of these two isomers in nonpolar capillary GC was also determined. However, the stereochemistry at C-9 and C-10 in the natural fatty acids will still remain unknown until a suitable analytical methodology is developed for the elucidation of the stereochemistry of internally methylated chiral carbons in fatty acids. Further work is in progress determining the structures of unusual marine dimethylated *iso*-branched fatty acids.

Experimental Section

General Experimental Procedures. IR spectra were recorded on a Nicolet 600 FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a General Electric Bruker DPX-300 or -500 spectrometer. ^{1}H NMR chemical shifts were recorded with respect to internal $(CH_3)_4Si$, and ^{13}C NMR chemical shifts are reported in parts per million relative to $CDCl_3$ (77.0 ppm). Fatty acid methyl esters were analyzed by GC−MS at 70 eV using a Hewlett-Packard 5972A MS ChemStation equipped with a 30 m × 0.25 mm special performance capillary column (HP-5MS) of polymethylsiloxane cross-linked with 5% phenyl methylpolysiloxane. HRMS data was obtained in a VG AutoSpec high-resolution mass spectrometer.

Animal Material. *C. podatypa* Van Soest (class Demospongiae, order Haplosclerida, family Phloeodictyidae) was collected near Mona Island, Puerto Rico, in 1992, at 20 m depth by scuba. A voucher specimen (no. MI-030) is stored at the Chemistry Department of the University of Puerto Rico, Río Piedras campus.

Isolation and Identification of Fatty Acids. The procedure for the extraction and identification of the phospholipid fatty acids from *C. podatypa* was described previously.[4]

6-Methyl-2-heptanone. Into a 25-mL round-bottomed flask were placed 15 mL of distilled MeOH, 0.65 g (5.2 mmol) of 6-methyl-5-hepten-2-one, and catalytic amounts of PtO_2. The mixture was allowed to react for 24 h under a hydrogen-filled balloon. Then, it was filtered and the solvent evaporated in vacuo, affording 0.60 g (91% yield) of the known saturated ketone.[7]

Methyl 8-Bromooctanoate. 8-Bromooctanoic acid (14.7 g, 66.2 mmol) and catalytic amounts of HCl were stirred in refluxing MeOH (25 mL) for 24 h. After this time, the solvent was removed in vacuo, affording 15.0 g (96% yield) of the known methyl ester, which was used in the next step without further purification.[8]

(7-Methoxycarbonylheptyl)triphenylphosphonium Bromide. To a stirred solution of triphenylphosphine (9.9 g, 37.6 mmol) in acetonitrile was slowly added methyl 8-bromooctanoate (7.6 g, 32.1 mmol). The mixture was refluxed under nitrogen for 36 h. After cooling, the acetonitrile was removed in vacuo, and the product was washed extensively with ether using ultrasound followed by decantation of the solvent to give the salt as a clear syrup (14.5 g, 90% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.87−7.67 (15H, m, $-C_6H_5$), 3.62 (3H, s, $-OCH_3$), 2.24 (2H, t, J = 7.4 Hz, H-2), 1.55 (6H, m, H-8, H-7, H-3), 1.25 (6H, m, H-4, H-5, H-6); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.2 (s,

C-1), 134.9 (s), 133.8 (d), 133.6 (d), 130.4 (d), 51.4 (q), 33.9 (t), 30.2 (t), 30.0 (t), 28.8 (t), 28.6 (t), 24.7 (t), 23.0 (t); HRFABMS *m*/*z* 499.1228 (calcd for $C_{27}H_{32}PO_2Br-H$, 499.1225).

Methyl 9,13-Dimethyl-8-tetradecenoate. To a flame-dried 50-mL three-necked round-bottom flask, equipped with a pressure-equalizing dropping funnel, a reflux condenser, and under a nitrogen atmosphere, was added 4.5 mL of anhydrous *t*-BuOH and 0.13 g (3.3 mmol) of potassium. After the potassium *t*-butoxide precipitated, the excess alcohol was removed with a double-ended syringe, and the phosphonium salt (1.6 g, 3.3 mmol), dissolved in THF, was then slowly added. After 10 min, 6-methyl-2-heptanone (0.09 g, 0.70 mmol) was also added to the reaction mixture. The reaction was allowed to stand overnight, and then it was quenched with a saturated ammonium chloride solution (25 mL), extracted with ether (2 × 50 mL), and dried over Na_2SO_4. After evaporation of the solvent in vacuo, the crude product was chromatographed on Si gel, eluting with hexane−ether (8:2, v/v), and this afforded the desired product [0.13 g, 73% yield of a mixture of 1.4:1 (*Z*/*E*)-isomers]: IR (neat) ν_{max} 2958 (=CH), 2930, 2857, 1737 (C=O), 1622, 1465, 1384, 1366, 1261, 1171, 1091, 1024, 876, 806, 725 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.09 [1H, t, J = 7.0 Hz, H-8, (*E*) and (*Z*)], 3.66 [3H, s, $-OCH_3$, (*E*) and (*Z*)], 2.30 [2H, t, J = 7.5 Hz, H-2, (*E*) and (*Z*)], 1.99−1.90 [4H, m, H-7, H-10, (*E*) and (*Z*)], 1.66 [3H, s, Me-9, (*Z*)], 1.65 [3H, s, H-3, H-13, (*E*) and (*Z*)], 1.57 [3H, s, Me-9, (E)], 1.36−1.25 [10H, m, (*E*) and (*Z*)], 0.87 [6H, d, J = 6.6 Hz, H-14, Me-13, (*Z*)], 0.86 [6H, d, J = 6.6 Hz, H-14, Me-13, (*E*)]; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.4 [s, C-1, (*E*) and (*Z*)], 135.5 [s, C-9, (*Z*)], 135.5 [s, C-9, (*E*)], 125.0 [d, C-8, (*Z*)], 124.3 [d, C-8, (*E*)], 51.4 [q, $-OCH_3$, (*E*) and (*Z*)], 39.9 [t, C-10, (*E*)], 38.9 [t, C-10, (*Z*)], 38.7 [t, C-12, (*E*)], 38.6 [t, C-12, (*Z*)], 34.0 [t, C-2, (*E*) and (*Z*)], 29.1 [t, (*E*) and (*Z*)], 29.0 [t, (*E*) and (*Z*)], 28.9 [t, (*E*) and (*Z*)], 27.9 [t, C-7, (*Z*)], 27.7 [t, C-7, (*E*)], 25.8 [t, (*E*) and (*Z*)], 25.7 [t, (*E*) and (*Z*)], 24.9 [t, (*E*) and (*Z*)], 23.7 [q, Me-9, (*E*)], 23.4 [q, Me-9, (*Z*)], 22.6 [q, C-14, Me-13, (*E*) and (*Z*)].

Methyl 9,13-dimethyl-8(*Z*)-tetradecenoate: t_R = 12.79 min, GC−MS (70 eV) *m*/*z* 268 [M^+] (18), 237 (10), 183 (10), 166 (17), 151 (23), 143 (33), 133 (10), 126 (45), 125 (13), 124 (12), 123 (16), 111 (39), 110 (18), 109 (22), 98 (12), 97 (23), 96 (16), 95 (20), 87 (17), 83 (63), 81 (34), 79 (13), 74 (21), 70 (37), 69 (94), 67 (38), 57 (35), 55 (100).

Methyl 9,13-dimethyl-8(*E*)-tetradecenoate: t_R = 12.99 min, GC−MS (70 eV) *m*/*z* 268 [M^+] (18), 237 (10), 166 (16), 151 (21), 143 (20), 126 (41), 125 (11), 124 (11), 123 (14), 111 (35), 110 (17), 109 (20), 98 (11), 97 (21), 96 (15), 95 (19), 87 (15), 83 (59), 81 (32), 79 (12), 74 (20), 70 (35), 69 (90), 67 (38), 57 (34), 55 (100).

Methyl 9,13-Dimethyltetradecanoate (1). Into a 25-mL round-bottom flask was placed 0.019 g (0.07 mmol) of methyl 9,13-dimethyl-8-tetradecenoate in 10 mL of distilled MeOH together with catalytic amounts of PtO_2. After 24 h under a hydrogen-filled balloon the reaction mixture was filtered and the solvent evaporated in vacuo, affording the saturated methyl ester **1** (0.019 g, 100% yield): ^1H NMR ($CDCl_3$, 500 MHz) δ 3.66 (3H, s, $-OCH_3$), 2.30 (2H, t, J = 7.6 Hz, H-2), 1.61 (2H, m, H-3), 1.51 (1H, m, H-13), 1.35−1.21 (15H, m), 1.14−1.11 (2H, m, H-12), 0.86 (6H, d, J = 6.6 Hz, Me-13, H-14), 0.83 (3H, d, J = 6.6 Hz, Me-9); ^{13} C NMR ($CDCl_3$, 125 MHz) δ 174.4 (s, C=O), 51.5 (q, $-OCH_3$), 39.3 (t), 37.3 (t), 37.0 (t), 34.1 (t), 32.7 (d, C-9), 29.3 (t), 29.2 (t), 28.1 (t), 28.0 (d, C-13), 27.0 (t), 24.9 (t), 24.8 (t), 22.7 (q, C-14), 22.6 (q, C-15), 19.7 (q, Me-9); GC−MS (70 eV) *m*/*z* 270 [M^+] (8), 171 (13), 153 (6), 143 (16), 135 (6), 115 (7), 111 (8), 101 (9), 97 (13), 86 (62), 83 (16), 75 (20), 74 (100), 71 (24), 69 (34), 67 (6), 57 (47), 55 (51).

***N*-9,13-Dimethyltetradecanoylpyrrolidine:** GC−MS (70 eV) *m*/*z* 309 $[M]^+$ (2), 294 (1), 280 (0.1), 266 (1), 252 (0.3), 238 (1), 224 (1), 210 (0.2), 196 (3), 182 (1), 168 (2), 154 (1), 140 (3), 126 (17), 114 (8), 113 (100), 98 (9), 85 (6), 71 (11), 70 (14), 57 (8), 56 (7), 55 (19).

(9-Hydroxynonyl)triphenylphosphonium Bromide. This compound was prepared from triphenylphosphine (13.9 g, 53 mmol) and 9-bromo-1-nonanol (11.8 g, 53 mmol), in benzene, following the same procedure as detailed above for the other salt. The salt was obtained as a clear syrup[11] (18.1 g, 71% yield): ^1H NMR ($CDCl_3$, 300 MHz) δ 7.87−7.68 (15H, m, C_6H_5), 3.59 (2H, t, J = 6.5 Hz, H-1), 1.62 (2H, br s, H-9), 1.49 (2H, m, H-2), 1.23 (12H, m, CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.0 (s), 133.6 (d), 130.5 (d), 130.4 (d), 62.6 (t, C-1), 32.5 (t), 30.2 (t), 28.9 (t), 28.8 (t), 28.7 (t), 25.4 (t), 22.6 (t), 22.5 (t).

10,13-Dimethyl-9-tetradecen-1-ol. This compound was prepared from (9-hydroxynonyl)triphenylphosphonium bromide (17.0 g, 35 mmol) and 5-methyl-2-hexanone (3.9 g, 34 mmol), in THF, using potassium *t*-butoxide (7.8 g, 70 mmol) as base, following the procedure described above for the synthesis of the other isomer. The desired product [5.6 g, 69% yield of a 1:1 mixture of (*Z*/*E*)-isomers] was obtained after evaporation of the solvent in vacuo and purification using Si gel column chromatography (hexane−ether, 8:2): IR (neat) ν_{max} 3500−3100 (OH), 2957, 2924, 2858, 1664 (C=C), 1463, 1384, 1367, 1116, 1057, 723 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.10 [1H, m, H-9, (*E*) and (*Z*)], 3.63 [2H, t, J = 6.6 Hz, H-1, (*E*) and (*Z*)], 2.00−1.95 [5H, m, H-8, H-11, O*H* (*E*) and (*Z*)], 1.66 [3H, s, Me-10, (*Z*)], 1.57 [3H, s, Me-10, (*E*)], 1.57−1.49 [3H, m, H-2, H-13, (*E*) and (*Z*)], 1.29−1.19 [12H, m, CH_2, (*E*) and (*Z*)], 0.89−0.87 [6H, d, J = 6.3 Hz, H-14, Me-13, (*E*) and (*Z*)]; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.7 [s, C-10, (*E*)], 135.4 [s, C-10, (*Z*)], 124.9 [d, C-9, (*E*)], 124.3 [d, C-9, (*Z*)], 63.1 [t, C-1, (*E*) and (*Z*)], 37.6 [t, C-11, (*E*)], 37.4 [t, C-12, (*Z*)], 37.3 [t, C-12, (*E*)], 32.8 [t, C-2, (*E*) and (*Z*)], 30.1 [t, (*E*) and (*Z*)], 29.9 [t, (*E*) and (*Z*)], 29.7 [d, C-13, (*E*) and (*Z*)], 29.7 [t, C-11, (*Z*)], 29.5 [t, (*E*) and (*Z*)], 29.4 [t, (*E*) and (*Z*)], 29.3 [t, (*E*) and (*Z*)], 28.1 [t, C-8, (*E*)], 27.9 [t, C-8, (*Z*)], 25.7 [t, (*E*) and (*Z*)], 23.5 [q, Me-10, (*E*) and (*Z*)], 22.6 [q, C-14, Me-13, (*E*) and (*Z*)]; HREIMS *m*/*z* 240.2459 (calcd for $C_{16}H_{32}O$, 240.2453).

10,13-Dimethyl-9(*Z*)-tetradecen-1-ol: t_R = 12.56 min, GC−MS (70 eV) *m*/*z* 240 [M^+] (9), 185 (1), 156 (1), 123 (11), 112 (10), 110 (19), 109 (23), 97 (16), 96 (22), 95 (37), 83 (33), 82 (46), 81 (41), 79 (11), 71 (11), 70 (21), 69 (100), 68 (30), 67 (49), 57 (66), 56 (73), 55 (98).

10,13-Dimethyl-9(*E*)-tetradecen-1-ol: t_R = 12.76 min, GC−MS (70 eV) *m*/*z* 240 [M^+] (9), 185 (1), 151(4), 123 (11), 112 (10), 110 (20), 109 (23), 97 (15), 96 (22), 95 (37), 83 (34), 82 (49), 81 (42), 79 (10), 71 (11), 70 (21), 69 (100), 68 (32), 67 (51), 57 (68), 56 (79), 55 (99).

10,13-Dimethyltetradecan-1-ol. This product was obtained in a 100% yield from the catalytic hydrogenation (PtO_2) of 10,13-dimethyl-9-tetradecen-1-ol (0.93 g, 3.88 mmol) using the same procedure as described above for the other isomer: IR (neat) ν_{max} 3500−3100 (OH), 2960, 2934, 2857, 1464, 1383, 1377, 1366, 1116, 1059, 716 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.62 (2H, t, J = 6.6 Hz, H-1), 1.85 (1H, s, −OH), 1.57−1.47 (3H, m, H-2, H-13), 1.29−1.07 (19H, m, CH_2), 0.86 (3H, d, J = 6.6 Hz, H-14), 0.85 (3H, d, J = 6.6 Hz, Me-13), 0.82 (3H, d, J = 6.4 Hz, Me-10); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 63.0 (t, C-1), 37.0 (t), 36.3 (t), 34.7 (t), 33.0 (t), 32.7 (d), 30.0 (t), 29.6 (t), 29.4 (d), 28.3 (t), 27.1 (t), 25.7 (t), 22.8 (t), 22.6 (q), 19.7 (q); GC−MS (70 eV) *m*/*z* 242 [M^+] (0.02), 241 (0.09), 224 (0.2), 210 (0.06), 196 (0.5), 181 (0.4), 168 (11), 153 (10), 140 (10), 125 (15), 112 (15), 97 (39), 83 (39), 69 (48), 57 (100); HREIMS *m*/*z* 224.2499 [$M^+ - H_2O$] (calcd for $C_{16}H_{32}$, 224.2504).

Methyl 10,13-Dimethyltetradecanoate (2). To a solution of pyridinium dichromate (2.2 g, 5.9 mmol) dissolved in DMF (20 mL) was added 10,13-dimethyltetradecanol (0.26 g, 1.08 mmol) dissolved in DMF (5 mL). The mixture was allowed to react for 20 h. The reaction mixture was then quenched with water, extracted with ether, and dried over Na_2SO_4. The product thus obtained was immediately reacted with catalytic amounts of HCl in refluxing MeOH (25 mL) for 24 h. After this time the solvent was removed in vacuo, affording only traces of the known saturated methyl ester **2** together with residual aldehyde.[5]

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References and Notes

(1) Djerassi, C.; Lam, W.-K. *Acc. Chem. Res.* **1991**, *24*, 69−75.
(2) Carballeira, N. M.; Reyes, E. D.; Sostre, A.; Rodríguez, A. D.; Rodríguez, J. L.; González, F. A. *J. Nat. Prod.* **1997**, *60*, 502−504.
(3) Nemoto, T.; Yoshino, G.; Ojika, M.; Sakagami, Y. *Tetrahedron* **1997**, *53*, 16699−16710.
(4) Carballeira, N. M.; Pagán, M.; Rodríguez, A. D. *J. Nat. Prod.* **1998**, *61*, 1049−1052.
(5) Carballeira, N. M.; Maldonado, M. E. *Lipids* **1989**, *24*, 371−374.
(6) Hattori, M.; Miyachi, K.; Hada, S.; Kakiuchi, N.; Kiuchi, F.; Tsuda, Y.; Namba, T. *Chem. Pharm. Bull.* **1987**, *35*, 3507−3510.
(7) Miller, K. V.; Jemiolo, B.; Gassett, J. W.; Jelinek, I.; Wiesler, D.; Novotny, M. *J. Chem. Ecol.* **1998**, *24*, 673−683.
(8) Cravatt, B. F.; Lerner, R. A.; Boger, D. L. *J. Am. Chem. Soc.* **1996**, *118*, 580−590.
(9) Mori, K.; Wu, J. *Liebigs Ann. Chem.* **1991**, *8*, 783−788.
(10) Kochansky, J.; Aldrich, J. R.; Lusby, W. R. *J. Chem. Ecol.* **1989**, *15*, 1717−1728.
(11) Wang, Q.; He, M.; He, X.; Yuan, G. *Rapid Commun. Mass Spectrom.* **1997**, *11*, 1728−1730.

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