Oligomeric Acylphloroglucinols from Myrtle (*Myrtus communis*)

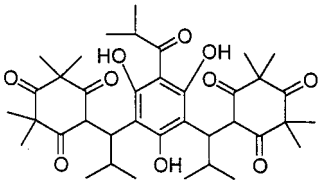
Giovanni Appendino,*,† Federica Bianchi,† Alberto Minassi,† Olov Sterner,*,‡ Mauro Ballero,§ and Simon Gibbons||

DISCAFF, Università del Piemonte Orientale, Viale Ferrucci 33, 28100 Novara, Italy, Department of Organic and Bioorganic Chemistry, Lund University, P.O.B. 124, 221 00 Lund, Sweden, Dipartimento di Scienze Botaniche, Universitá degli Studi di Cagliari, Viale San Ignazio 13, 09123 Cagliari, Italy, and Centre for Pharmacognosy and Phytotherapy, The School of Pharmacy, University of London, London, WC1N 1AX England

Received September 7, 2001

The dimeric nonprenylated acylphloroglucinol semimyrtucommulone (**6**) was obtained from the leaves of myrtle (*Myrtus communis*) as a 2:1 mixture of two rotamers. The known trimeric phloroglucinol myrtucommulone A (**1**) was also isolated and characterized spectroscopically as a silylated cyclized derivative (**5**). Myrtucommulone A showed significant antibacterial activity against multidrug-resistant (MDR) clinically relevant bacteria, while semimyrtucommulone was less active.

Myrtle (*Myrtus communis* L., Myrtaceae) is the archetypal Mediterranean species, and its relevance in medicine, cuisine, and art as well as in religion and myth can hardly be overstated.[1] Current economic interest focuses on the berries and the leaves, which are used to make a popular liqueur and as a hop substitute for beer,[2] but several investigations have evidenced the strong antibacterial activity of myrtle leaf extracts,[3] supporting the use of this plant as an antiseptic in traditional Mediterranean medicine.[4] Phytochemical investigations spanning several decades afforded various monoterpenoids, flavonoids, and triterpenes,[5] but the identity of the antibacterial principle has long remained elusive. In the mid 1970s, Israeli scientists eventually reported the isolation of a phloroglucinol antibiotic from the leaves of myrtle. This compound was named myrtucommulone A (**1**) and was obtained as a



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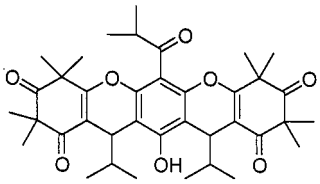

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mixture of homologues and tautomers which was not amenable to a detailed NMR analysis.[6] Related compounds were also obtained,[6,7] and one of them, the dimer myrtucommulone B (**3**), has recently raised interest for the treatment of psoriatic disorders.[8] We present here the characterization of a new dimeric nonprenylated phloroglucinol from myrtle, the spectroscopic characterization of myrtucommulone A as a silylated cyclized derivative, and the disclosure of its significant activity against multidrug-resistant bacteria.

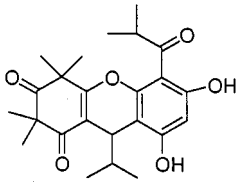
Results and Discussion

An acetone extract from the dried leaves of myrtle was fractionated by open CC to afford two phloroglucinol mixtures. The MS of the least polar and abundant (0.14%) fraction showed a cluster of five molecular ion peaks spaced by 14 mass units in an approximate ratio of 12:4:2:1:1, indicating a mixture of homologues. The NMR spectrum in a variety of solvents showed only unresolved peaks and was of little use for structure elucidation. Repeated crystallizations eventually removed the minor homologues and afforded a ca. 7:1 mixture (MS analysis) of two compounds, having EIMS and mp identical to those reported for myrtucommulone A (**1**).[6] The structure of this compound was established mainly on the basis of MS data,[6] with additional support from the acid-catalyzed cyclization to a bis-pyrane derivative (**2**) amenable to NMR investigation.[6b] The acidic treatment of our compound gave a complex mixture, and we tried therefore to confirm its identity with myrtucommulone A (**1**) using variable-temperature NMR experiments and an alternative derivatization strategy. Our compound proved too unstable for high-temperature NMR measurements. Thus, heating in DMSO at 80 °C for 24 h afforded a mixture of two compounds, a dimer (**4**) isomeric with myrtucommulone B (**3**) and a trimer related to the bis-dehydrated product **2**. In our hands, the two compounds could not be separated, and their structure was determined from the NMR analysis of the mixture. Owing to severe overlapping of many signals, it was not possible to fully characterize the trimeric product. However, the ^{13}C NMR spectrum showed that the central aromatic ring was not symmetric, thus suggesting an angular (cf. **5**) rather than a linear (**2**) structure. The formation of the dimer **4** was followed monitoring the upfield signal for H-5, while the substitution pattern of the benzene ring was established by HMBC correlations. The absence of a signals for 6-OH and 6′-OH and NOESY correlations between H-5 and 4-OH as well as the 14′-methyl supported a tricyclic structure, isomeric with myrtucommulone B, for **4**. It should be noted that the published NMR data for myrtucommulone B[6b] do not distinguish between structures **3** and

* To whom correspondence should be addressed. Tel (G.A.): +39 011 670 7684; (O.S.): +46 4622 28213. Fax (G.A.): + 39 011 670 7687; (O.S.): +46 4622 28213. E-mail (G.A.): appendin@pharm.unito.it; (O.S.): Olov.Sterner@orgk2.lth.se.
† DISCAFF, Università del Piemonte Orientale.
‡ Lund University.
§ Universitá degli Studi di Cagliari.
|| University of London.

10.1021/np010441b CCC: $22.00 © 2002 American Chemical Society and American Society of Pharmacognosy
Published on Web 02/19/2002

4, and the possibility that this compound might actually be reformulated as **4** should not be neglected. In this case, the facile transformation of **1** to **4** makes it possible that myrtucommulone B is an artifact of extraction and/or isolation.



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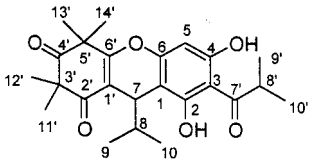

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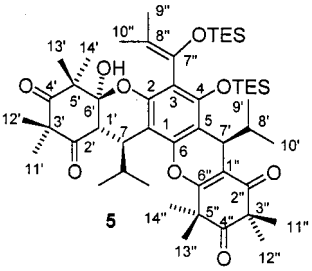

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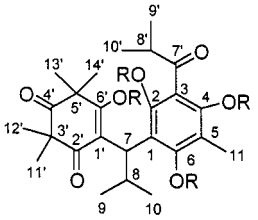
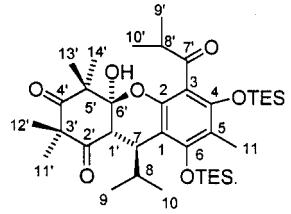
Acetylation and methylation of **1** gave complex mixtures, but silylation eventually delivered, in modest yield (23%), a derivative that maintained the carbon−carbon connectivity of the natural product and was amenable to spectroscopic analysis. The molecular formula of **5** ($C_{50}H_{78}O_9Si_2$) evidenced the presence of two −OTES groups, while careful analysis of the 2D NMR data settled unambiguously the structure and configuration. Surprisingly, the pentacyclic angular enol ether **5** was obtained in a configurationally unitary form and free from homologues. This structure is the one expected for a compound formed from the bisacetalization, the monodehydration, and the disilylation of a starting material having the bona fide formula of myrtucommulone A and is consequently complementing the previous structural identification based on the MS data. As to the site(s) of homologation of myrtucommulone A, the cluster of homologous peaks observed for the parent ion was also present in the mass peak resulting, after dehydration, from the α-cleavage of the isobutyryl group [M − C_3H_7 − H_2O], suggesting that homologation occurs at the isobutylidene bridge(s). The tautomeric composition of myrtucommulone A remains unknown. On the basis of previous studies of the prototropic equilibria in benzyl-substituted syncarpic acids,[9] several plausible tautomeric forms can be envisaged for myrtucommulone A, with formula **1** representing only one of the three possibilities where aromaticity of the central ring is maintained.

The more polar and abundant phloroglucinol **6**, named semimyrtucommulone, was obtained free from homologues. HRMS data established the molecular formula $C_{25}H_{34}O_7$, while the NMR spectra showed duplication of all resonances. The failure to evidence two compounds by HPLC techniques and the coalescence of the NMR signals at 90 °C indicated that **6** was a mixture of two tautomers or rotamers, in a ratio of ca. 2:1 at room temperature. The two sets of ^{1}H NMR signals showed the same proton spin systems (one isobutylidene group, one isopropyl, four methyls bound to nonprotonated aliphatic carbons, and one benzylic methyl), suggesting that the equilibrating species were rotamers rather than tautomers. Due to the high number of nonprotonated carbons, HMBC experiments were utilized extensively to correlate the ^{1}H and ^{13}C resonances and assemble them into the same dimeric phloroglucinol structure **6**. Again, correlations from the hydroxyl protons as well as from the methyl protons revealed the carbon skeleton of **6**. Silylation afforded a ca. 1:1 mixture of two isomeric cyclized derivatives, identified as **7** and **8**. HRMS experiments revealed the same elemen-



R
6 H
6a Ac



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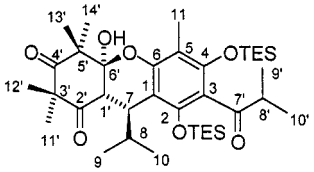

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tal composition for these compounds. The unsaturation index, along with the NMR data, suggested that they are tricyclic derivatives, similar to compound **5**. NOESY correlations were used to distinguish between the two compounds. Thus, while the benzylic 11-methyl of **7** correlated with the methylene protons of both TES groups, in **8** the correlation with one of the TES groups was replaced by that with the 11-methyl. In addition, the signal for the hemiacetal proton in **8** was sufficiently resolved to give a NOESY correlation to the 14′-methyl and HMBC correlations to C-1′, C-5′, and C-6′. In both compounds, H-1′ gave NOESY correlations with the 12′-, 13′-, 9-, and 10-methyls, establishing the relative configuration. Remarkably, both compounds were configurationally pure, confirming the surprising capacity of oligomeric phloroglucinols to form polycyclic structures in a highly stereoselective way. Also noteworthy is the observation that, while the silylation of myrtucommulone A (**1**) yielded only one isomer, two isomers were instead formed from semimyrtucommulone (**6**). A possible explanation is that the phenolic hydroxyl in the linear trimeric assembly corresponding to **7** (that is, **2**) is sterically more encumbered than in the corresponding angular assembly like **5** (corresponding to **7**) and, thus, essentially unreactive with the bulky silylating agent. Acetylation of **6** gave one product (**6a**), identified by MS

Table 1. Minimum Inhibitory Concentrations (MIC) of **1** and **6** against Various *Staphylococcus aureus* Strains

bacterial strain (MDR efflux system)	MIC (μg/mL)		
	1	**6**	tetracycline
RN4220 (Msr(A))[a]	0.5	32	0.5
XU212 (Tet(K))[b]	1	32	256
1199-B (Nor(A))[c]	1	32	32
ATCC 25923[d]	2	64	0.5

[a] Macrolides resistant. [b] Tetracyclines resistant. [c] Fluoroquinolones resistant. [d] Standard ATCC strain.

as a tetraacetate derivative of the natural product. The ^{1}H NMR spectrum taken at 500 MHz was poorly resolved, temperature dependent, and not suitable for structural identification. As expected for a dynamic equilibrium, a decrease of the instrumental frequency improved the resolution, and at 50 °C and 200 MHz most peaks of the ^{1}H NMR spectrum could be assigned. Since acetylation blocks prototropic equilibria, the detection of a dynamic process in the peracetyl derivative of **6** further confirmed that the duplication of the resonances in the NMR spectra of the natural product is due to a conformational process. The differences in NOESY pattern between the two rotamers of **6** could not be easily translated into definite arrangements around the bonds 1′−7 and 1−7, where hindered rotation seems most likely to occur. The discovery of a slow rotameric equilibrium in alkylidene-bridged phloroglucinyl−syncarpyl dimers makes factorial the problem of the characterization of **1**, suggesting that this compound, apart from the tautomeric equilibration typical of syncarpic acid derivatives,[8] can also undergo conformational equilibration.

A biological evaluation of **1** and **6** showed activity against clinically relevant microorganisms. The minimum inhibitory concentrations[10] of **1** and **6** were determined against strains of multidrug-resistant (MDR) *Staphylococcus aureus* which possessed efflux mechanisms of resistance to macrolides, tetracyclines, and fluoroquinolones via the Msr(A),[11] Tet(K),[12] and Nor(A)[13] transporters, respectively (Table 1). Myrtucommulone (**1**) showed a submicromolar or low micromolar activity against all the bacteria investigated, while semimyrtucommulone was 30−60-fold less active. Interestingly, the strains investigated were more susceptible to these agents than a standard ATCC strain, possibly indicating that these phloroglucinols are not substrates of multidrug efflux. Further work is underway to assess whether these compounds are inhibitors of these efflux mechanisms, which would also account for the potent activity observed against these MDR strains. Given the current shortage of efficient antibacterial agents against MDR bacteria, myrtucommulone A qualifies as a new and interesting lead for drug discovery.

The unifying feature of myrtle phloroglucinols is the presence of a fully substituted phloroglucinol core bound via isobutylidene bridge(s) to syncarpyl moiety(ies). The lack of prenylation sets these compounds apart from plant phloroglucinols,[14] while substitution at the phloroglucinol−syncarpyl bridge clearly distinguishes them from fern phloroglucinols.[15]

In conclusion, the leaves of myrtle provide access to unique chemical diversity, whose involvement in the antibacterial activity of the plant seems well established. Apart from the antibiotic properties, myrtle extracts show also powerful hypoglycemic activity[16] and can inhibit aryl hydrocarbon hydroxylase,[17] two activities of pharmacological interest in the realm of diabetes and chemoprevention. Further studies are, however, necessary to assess if also these properties can be traced back to the unique phloroglucinol constituents of the plant.

Experimental Section

General Experimental Procedures. IR spectra were recorded on a Shimadzu DR 8001 spectrophotometer. HRMS (EI, 70 eV) were taken on VG 7070 EQ and JEOL SX102 spectrometers. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker DRX-500 spectrometer (500 and 125 MHz, respectively) equipped with a Bruker ARX500 spectrometer with an inverse multinuclear 5 mm probehead equipped with a shielded gradient coil. The ^{1}H NMR spectrum of **6a** was recored on a Bruker AM 200 spectrometer (200 MHz). The solvent signals ($CHCl_3/CDCl_3$ 7.26/77.0 ppm, DMSO-d_6 2.50/39.5 ppm) were used as internal reference. The chemical shifts (δ) are given in ppm, and the coupling constants (J) in Hz. COSY, HMQC, and HMBC experiments were recorded with gradient enhancements using sine-shaped gradient pulses. For the 2D heteronuclear correlation spectroscopy the refocusing delays were optimized for $^1J_{CH} = 145$ Hz and $^nJ_{CH} = 10$ Hz. The raw data were transformed and the spectra were evaluated with the standard Bruker XWIN-NMR software (rev. 010101). HRMS (EI, 70 eV) and CIMS were taken on a VG 7070 EQ spectrometer. HRFABMS were taken on a JEOL SX102 spectrometer. Silica gel 60 (70−230 mesh, Merck) and LiChroprep RP-18 (25−40 μM) were used for open-column chromatography (CC). A Waters Microporasil semipreparative column (0.8 × 30 cm) was used for HPLC, with detection by a Waters differential refractometer 340.

Plant Material. Various samples of *Myrtus communis* L. were collected in Sardinia during the years 1999−2001. The extraction and isolation procedure reported refers to a sample collected at Corongiu (Laconi, NU) on November 12, 2000. The plant was identified by M.B., and a voucher specimen (CAG 514) is deposited at the Dipartimento di Scienze Botaniche, Università di Cagliari.

Extraction and Isolation. Dried and powdered leaves (1 kg) were extracted with acetone at room temperature (4 × 3 L). Evaporation of the pooled extracts left a green gum, which was taken up in ethanol (1 L) and treated with an equal volume of 3% aqueous lead(II) acetate. After resting overnight, the solution was filtered over a bed of Celite (ca. 20 g), concentrated to ca. 500 mL, and diluted with water (500 mL). The mixture was extracted with EtOAc (4 × 300 mL), and the pooled organic phases were dried (Na_2SO_4) and evaporated to give 18 g (1.8%) of a green paste. A portion of this (15 g) was chromatographed on a Florisil column (250 g) packed with petroleum ether−EtOAc, 95:5, and eluted with a petroleum ether−EtOAc gradient. Fractions eluted with 9:1 petroleum ether−EtOAc gave a semisolid residue, which was washed with ether to afford 0.9 g of myrtucommulone A (**1**) as a yellow powder. Fractions eluted with 5:5 to 1:9 petroleum ether−EtOAc contained a mixture of myrtucommulone A and semimyrtucommulone and were further rechromatographed over Si gel (150 g, petroleum ether−EtOAc, 1:9) and then over RP-Si gel (30 g, MeOH−water, 8:2) to afford an additional 0.31 g of myrtucommulone A (overall yield 1.21 g, 0.12%) and 1.4 g (0.14%) of semimyrtucommulone (**6**).

Semimyrtucommulone (6): yellow powder, mp 147 °C; IR (KBr) ν_{max} 3501, 3517, 1707, 1614, 1470, 1385, 1289, 1157, 1020 cm^{-1}; ^{1}H NMR ($CDCl_3$) (major rotamer) δ 11.6 (1H, s, 4-OH), 10.5 (1H, s, 6′-OH), 5.46 (1H, s, 6-OH), 3.94 (1H, hept, $J = 6.8$ Hz, H-8′), 3.78 (1H, d, $J = 11.0$ Hz, H-7); 2.99 (1H, m, H-8); 2.09 (3H, s, H-11), 1.47 (3H, s, H-13′); 1.41 (3H, s, H-11′), 1.32 (3H, s, H-14′), 1.30 (3H, s, H-12′), 1.18 (6H, d, $J = 6.8$ Hz, H-9′ and H-10′), 0.83 (3H, d, $J = 6.4$ Hz, H-9), 0.72 (3H, d, $J = 6.4$ Hz, H-10); ^{13}C NMR ($CDCl_3$) (major rotamer) δ 212.7 (s, C-4′), 211.2 (s, C-7′), 203.2 (s, C-2′), 178.5 (s, C-6′), 161.6 (s, C-4), 160.8 (s, C-2), 156.0 (s, C-6), 114.2 (s, C-1′), 108.6 (s, C-1), 108.6 (s, C-5), 102.9 (s, C-3), 54.7 (s, C-3′), 48.9 (s, C-5′), 40.9 (d, C-7), 39.0 (d, C-8′), 26.5 (q, C-11′), 25.9 (q, C-13′), 25.8 (d, C-8), 24.8 (q, C-14′), 23.3 (q, C-12′), 22.0 (q, C-9), 21.8 (q,

C-10), 19.4 (q, C-9′), 19.3 (q, C-10′); HREIMS *m/z* 446.2288 $[M]^+$ (8) (calcd for $C_{25}H_{34}O_7$, 446.2304).

Thermal Degradation of Myrtucommulone (1). A sample of **1** in DMSO-d_6 was heated to 80 °C. The course of the degradation could be followed focusing on the upfield signal of H-5 (δ 6.24) and C-5 (δ 94.2) in the ^{1}H and ^{13}C NMR spectra, respectively. After 48 h the degradation was complete, and a mixture of isomyrtucommulone B (**4**) and a trimeric dehydration product was obtained. ^{1}H NMR data for **4**: ($CDCl_3$) δ 13.9 (1H, s, 2-OH), 11.2 (1H, s, 4-OH) 6.24 (1H, s, H-5), 4.12 (1H, d. J = 3.6 Hz, H-7), 3.91 (1H, hept., J = 6.8 Hz, H-8′), 1.85 (1H, m, H-8), 1.50 (3H, s, H-13′), 1.35 (3H, s, H-14′), 1.31 (3H, s, H-11′), 1.25 (3H, s, H-12′), 1.12 and 1.10 (2 × 3H, d, J = 6.8 Hz, H-9′ and H-10′), 0.69 (6H, d, J = 6.8 Hz, H-9 and H-10); ^{13}C NMR ($CDCl_3$) δ 211.5 (s, C-4′), 211.0 (s, C-7′), 196.9 (s, C-2′), 167.4 (s, C-6′), 162.4 (s, C-2), 159.7 (s, C-4), 156.5 (s, C-6), 110.9 (s, C-1′), 106.6 (s, C-3), 103.2 (s, C-1), 94.2 (d, C-5), 55.6 (s, C-3′), 46.8 (s, C-5′), 38.9 (d, C-8′), 35.0 (d, C-8), 31.2 (d, C-7), 25.2 (q, C-11′), 23.5 (q, C-12′), 25.0 (q, C-13′), 24.0 (q, C-14′), 19.2 (q, C-9), 18.8 (q, C-9′), 18.4 (q, C-10), 17.7 (q, C-10′).

Silylation of Myrtucommulone (1). To a suspension of **1** (200 mg) in dry CH_2Cl_2 (5 mL) were added an excess (20 molar equiv) of TES-Cl and imidazole. After stirring at room temperature overnight, the reaction was worked up by addition of Si gel 60 (1 g) and evaporation. The residue was purified twice by CC (Si gel, 5 g, petroleum ether−EtOAc, 95:5) to eventually afford 61 mg (23%) of **5** as an oil, along with 49 mg of recovered starting material. IR (liquid film) ν_{max} 3408, 1720, 1590, 1548, 1470, 1370, 1300, 1185, 1018 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.27 (1H, d, J = 3.3 Hz, H-7′), 4.17 (1H, dd, J = 5.9 and 3.6 Hz, H-7), 3.69 (1H, d, J = 5.9 Hz, H-1′), 2.71 (1H, s, 6′-OH), 2.57 (1H, m, H-8), 2.02 (1H, m, H-8′), 1.74 (3H, s, H-9″), 1.65 (3H, s, H-13″), 1.61 (3H, s, H-14″), 1.57 (3H, s, H-14′), 1.45 (3H, s, H-11″), 1.43 (3H, s, H-12′), 1.37 (3H, s, H-12″), 1.37 (3H, s, H-10″), 1.35 (3H, s, H-13′), 1.32 (3H, s, H-11′), 0.96 (2H, t, J = 8 Hz, 4-OTES), 0.94 (3H, d, J = 6.8 Hz, H-9), 0.89 (2H, t, J = 8 Hz, 7″-OTES), 0.83 (3H, d, J = 6.8 Hz, H-9′), 0.73 (3H, q, J = 8 Hz, 4-OTES), 0.67 (3H, d, J = 6.8 Hz, H-10), 0.61 (3H, d, J = 6.8 Hz, H-10′), 0.48 (3H, q, J = 8 Hz, 7″-OTES); ^{13}C NMR ($CDCl_3$) δ 214.2 (s, C-4′), 212.4 (s, C-4″), 205.4 (s, C-2′), 197.7 (s, C-2″), 168.6 (s, C-6″), 151.7 (s, C-4), 149.2 (s, C-6), 147.0 (s, C-2), 135.9 (s, C-7″), 117.9 (s, C-3), 112.4 (s, C-8″), 112.3 (s, C-1″), 109.6 (s, C-5), 108.8 (s, C-1), 98.9 (s, C-6′), 58.2 (s, C-3′), 56.1 (s, C-3″), 54.8 (s, C-5′), 47.6 (s, C-5″), 44.6 (d, C-1′), 34.1 (d, C-8′), 32.9 (d, C-7′), 31.6 (d, C-8), 29.7 (d, C-7), 27.3 (q, C-12′), 25.7 (q, C-13″), 25.4 (q, C-14″), 24.7 (q, C-11″), 24.6 (q, C-12″), 23.9 (q, C-14′), 21.7 (q, C-11′), 20.4 (q, C-10″), 20.4 (q, C-9′), 20.2 (q, C-9), 17.6 (q, C-13′), 16.9 (q, C-9″), 16.4 (q, C-10′), 15.8 (q, C-10), 6.8 and 6.7 (t, OTES), 5.4 and 5.1 (q, OTES); EIMS (70 eV) *m/z* 878 $[M]^+$ (2), 863 (3), 849 (19), 835 (100), 735 (13), 721 (12), 703 (9); diagnostic NOESY correlations H-1′/H-12′, H-1′/H-13′, H-1′/H-9, H-1′/H-10, H-9/13″-methyl, H-10/13″-methyl, H-7/14″-methyl; CIMS (NH_3) *m/z* 879 $[M + H]^+$ (73); HRFABMS (NaI added) *m/z* 901.5115 $[M + Na]^+$ (5) (calcd for $C_{50}H_{78}O_9Si_2Na$, 901.5082); HRFABMS (KBr added) *m/z* 917.4937 $[M + K]^+$ (10) (calcd for $C_{50}H_{78}O_9Si_2K$, 917.4821).

Acetylation of Semimyrtucommulone (6). To a solution of **6** (686 mg, mmol) in pyridine (4 mL) was added Ac_2O (4 mL). After stirring overnight at room temperature, the excess Ac_2O was quenched by the addition of MeOH (2 mL), and the reaction was worked up by dilution with 2 N H_2SO_4 and extraction with EtOAc. The organic phase was sequentially washed with 2 N H_2SO_4, water, saturated $NaHCO_3$, and brine. After drying (Na_2SO_4), removal of the solvent left a semisolid residue, which was purified by CC (15 g Si gel, petroleum ether−EtOAc, 95:5, as eluant) to afford, after crystallization from ether, 426 mg (45%) of **6a** as a white powder: mp 178 °C; IR (KBr) ν_{max} 1778, 1767, 1726, 1692, 1620, 1377, 1206, 1182, 1096, 1044 cm^{-1}; ^{1}H NMR ($CDCl_3$, 50 °C) δ 3.97 (1H, m, H-8′), 3.65 (1H, m, H-7); 2.86 (1H, m, H-8); 2.32, 2.30, 2.28, 2.24, 2.16 (each 3H, s, 4 × OAc and H-11), 1.37−1.22 (br m, H-11′, H-12′, H-13′, H-14′), 1.16 (6H, d, J = 7.0 Hz, H-9′ and H-10′), 0.85 (3H, d, J = 6.4 Hz, H-9), 0.67 (3H, d, J = 6.4 Hz, H-10); HREIMS *m/z* 614.2712 $[M]^+$ (2) (calcd for $C_{33}H_{42}O_{11}$, 614.2727).

Silylation of Semimyrtucommulone (6). To a solution of **6** (200 mg) in dry CH_2Cl_2 (5 mL) were added excess (12 molar equiv) TES-Cl and imidazole. After stirring at room temperature overnight, the reaction was worked up by addition of Si gel 60 (1 g) and evaporation. The residue was purified by CC (Si gel, 5 g, eluant petroleum ether−EtOAc, 95:5) to give a mixture of **7** and **8** (88 mg), which was further purified by HPLC (petroleum ether−EtOAc, 98:2) to afford 24 mg of **7** and 22 mg of **8** as colorless oils. Compound **7** was obtained as an oil: IR (liquid film) ν_{max} 3413, 1721, 1596, 1571, 1458, 1379, 1306, 1165, 1037 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.02 (1H, dd, J = 3.8 and 5.5 Hz, H-7), 3.52 (1H, d, J = 5.5 Hz, H-1′), 3.01 (1H, hept., J =7.0 Hz, H-8′), 2.44 (1H, m, H-8), 2.08 (3H, s, H-11), 1.79 (1H, brs, 6′-OH), 1.46 (3H, s, H-13′), 1.38 (3H, s, H-12′), 1.31 (3H, s, H-11′), 1.28 (3H, s, H-14′), 1.13 (3H, d, J = 7.0 Hz, H-9′), 1.12 (3H, d, J = 7.0 Hz, H-10′), 0.97 (3H, t, J = 8.1 Hz, 6-OTES), 0.91 (3H, t, J = 7.9 Hz, 4-OTES), 0.85 (2H, q, J = 8.1 Hz, 6-OTES), 0.84 (3H, d, J = 6.9 Hz, H-9), 0.67 (2H, q, J = 8 Hz, 4-OTES), 0.52 (3H, d, J = 6.8 Hz, H-10); ^{13}C NMR ($CDCl_3$) δ 215.0 (s, C-4′), 209.1 (s, C-7′), 205.7 (s, C-2′), 153.6 (s, C-2), 149.5 (s, C-4), 145.7 (s, C-6), 118.3 (s, C-3), 115.3 (s, C-5), 113.9 (s, C-1), 98.5 (s, C-6′), 58.0 (s, C-3′), 54.6 (s, C-5′), 45.7 (d, C-1′), 42.3 (d, C-8′), 30.9 (d, C-7), 30.3 (d, C-8), 27.2 (q, C-12′), 24.3 (q, C-13′), 21.9 (q, C-11′), 19.9 (q, C-9), 18.2 (q, C-9′), 18.1 (q, C-14′), 17.1 (q, C-10′), 16.0 (q, C-10), 11.6 (q, C-11), 6.7 (q, 6-OTES), 6.6 (q, 4-OTES), 5.5 (t, 6-OTES), 5.3 (t, 4-OTES); CIMS (NH_3): 675.4108 $[M + H]^+$ (100) (calcd for $C_{37}H_{63}O_7Si_2$, 675.4112), 645 (8%), 575 (17%), 561 (32%), 439 (24%), 325 (12%), 297 (10%). Compound **8** was also an oil: IR (liquid film) ν_{max} 3420, 1720, 1587, 1548, 1466, 1370, 1309, 1188, 1018 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.02 (1H, dd, J = 4.0 and 5.5 Hz, H-7), 3.62 (1H, d, J = 5.5 Hz, H-1′), 2.89 (1H, hept., J =7.0 Hz, H-8′), 2.60 (1H, brs, 6′-OH), 2.45 (1H, m, H-8), 2.03 (3H, s, H-11), 1.59 (3H, s, H-13′), 1.43 (3H, s, H-14′), 1.42 (3H, s, H-12′), 1.32 (3H, s, 11′), 1.10 (3H, d, J = 7.0 Hz, H-9′), 1.09, (3H, d, J = 7.0 Hz, H-10′), 0.91 (3H, t, J = 8.1 Hz, 6-OTES), 0.90 (3H, t, J = 7.9 Hz, 4-OTES), 0.84, (3H, d, J = 6.9 Hz, H-9), 0.80 (2H, q, J = 8 Hz, 6-OTES), 0.70 (2H, q, J = 8 Hz, 4-OTES), 0.52 (3H, d, J = 6.8 Hz, H-10; ^{13}C NMR ($CDCl_3$) δ 214.7 (s, C-4′), 209.0 (s, C-7′), 205.7 (s, C-2′), 149.7 (s, C-4), 149.4 (s, C-6), 148.4 (s, C-2), 122.0 (s, C-3), 113.0 (s, C-1), 112.4 (s, C-5), 98.2 (s, C-6′), 58.1 (s, C-3′), 54.4 (s, C-5′), 45.9 (d, C-1′), 42.2 (d, C-8′), 30.5 (d, C-7), 30.4 (d, C-8), 27.3 (q, C-12′), 24.3 (q, C-13′), 21.7 (q, C-11′), 19.9 (q, C-9), 18.3 (q, C-14′), 17.4 (q, C-9′), 17.2 (q, C-10′), 15.9 (q, C-10), 9.5 (q, C-11), 6.6 (q, 6-OTES), 6.6 (q, 4-OTES), 5.3 (t, 6-OTES), 5.0 (t, 4-OTES); CIMS (NH_3) *m/z* 675.4071 $[M + H]^+$ (100) (calcd for $C_{37}H_{63}O_7Si_2$, 675.4112), 659 (28), 645 (88), 561 (32), 543 (9), 493 (13), 463 (14), 439 (4), 325 (5), 297 (6), 237 (36).

Acknowledgment. We are grateful to Mrss. Sabrina Frongia and Silvia Turaglio and for their help throughout this investigation. We also thank also Dr. Luisella Verotta (University of Milano) for her helpful suggestions. This work was supported by EU (Contract ERB FAIR CT 1781) and MURST (Fondi 40%, Progetto Chimica dei Composti Organici di Interesse Biologico).

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NP010441B