A Concise Synthesis of Siphonodictidine†

Charles W. Jefford,* Jean-Claude Rossier, John Boukouvalas, Adam W. Sledeski, and Ping-Zhong Huang

Department of Organic Chemistry, University of Geneva, 30 quai Ernest-Ansermet, 1211 Geneva 4, Switzerland

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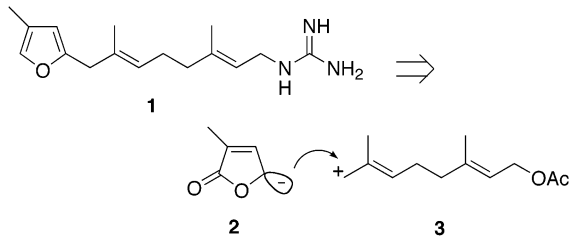
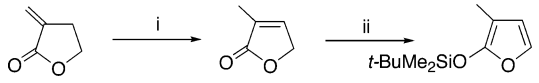
Siphonodictidine (**1**) has been synthesized for the first time in a concise and regiocontrolled manner by using 2-(*tert*-butyldimethylsiloxy)-3-methylfuran (**6**) as the crucial building block. The silver trifluoroacetate-induced alkylation of **6** with ω-bromogeranyl acetate **7** gave the key γ-lactone intermediate **8**, which on subsequent reduction, conversion of the hydroxyl into the amino group, and amidination afforded siphonodictidine (**1**) in an overall yield of 25.7% from **6**.

Siphonodictidine (**1**) is the secondary metabolite of an Indo-Pacific sponge *Siphonodictyon* sp.,[1] which burrows into living coral. It belongs to an extensive family of naturally occurring sesquiterpenes, which are characterized by a 2(5*H*)-furanone ring bearing a methyl group and an allylic attachment at the C3 and C5 positions, respectively. Among the members of this class discovered so far,[2,3] siphonodictidine is remarkable for its biological action.[1] It inhibits growth of the coral and appears to be deployed by the sponge to kill coral polyps in its immediate vicinity. Apart from this specific function, which is essential for the survival of the sponge, siphonodictidine exhibits significant antifungal and antimicrobial activity against Gram-positive and Gram-negative bacteria. Consequently, these potentially valuable properties and the fact that siphonodictidine (**1**) is only obtainable in minute amounts from undependable natural sources make it a suitable synthetic target.[4]

Scheme 1



Scheme 2[a]



[a] (i) $RhCl_3 \cdot 3H_2O$, EtOH, 100 °C, 3 h; (ii) TBDMSOTf, Et_3N, Et_2O, 0 to 23 °C, 24 h.

Results and Discussion

Despite the apparently simple structure of such furanosesquiterpenes, little attention has been paid to their synthesis.[5] Inspection of the farnesene backbone of **1** suggests that it could be conveniently assembled by coupling the C-5 carbanion **2** of 3-methyl-2(5*H*)-furanone (**5**) with the terminal cation **3** of geranyl acetate. Once the carbon skeleton is put in place, subsequent modification of the lactone ring and conversion of the acetate group into the guanidine entity would furnish **1** (Scheme 1). Unfortunately, the behavior of 2-furanolate ions is inconsistent. For example, the lithium enolate obtained from **5** on alkylation with various allyl bromides gives both C-3- and C-5-substituted products, with the former predominating.[6] However, we and others have already demonstrated that the desired C-5 regioselectivity can be conferred by recourse to 2-(trialkylsiloxy)furans, which behave as the equivalent of the localized C-5 carbanion of the 2(5*H*)-furanone entity. Applications involving vinylogous Mannich reactions, aldol-type coupling, and alkylation are well documented.[7−10]

In the present instance, the reagent of choice for synthon **2** is 2-(*tert*-butyldimethylsiloxy)-3-methylfuran (**6**).[11] The starting material selected for **6** is the commercially available α-methylene-γ-butyrolactone (**4**). Isomerization with rhodium chloride trihydrate afforded 3-methyl-2(5*H*)-furanone (**5**) in 86.6% yield.[12] Treatment of **5** with *tert*-butyldimethylsilyl trifluoromethanesulfonate and triethylamine furnished **6** in 88.5% yield (Scheme 2). Unlike 3-methyl-2-trimethylsiloxyfuran,[13] **6** is virtually impervious to moisture and can be easily purified by distillation or chromatography over silica gel.

An appropriate reagent for synthon **3** is ω-bromogeranyl acetate (**7**), a known compound obtainable from geranyl acetate by ω-hydroxylation and subsequent bromination.[14] At first sight, nucleophilic displacement could occur at either of the allylic positions.[15] But it will be seen shortly that activation with silver salt provides the desired selectivity.

Having the essential reagents **6** and **7** in hand, the next step is to put them together to create the carbon framework of siphonodictidine (**1**). Coupling was achieved by treatment with a stoichiometric amount of silver trifluoroacetate (Scheme 3). In keeping with previous findings,[10,11] alkylation occurred with high regioselectivity, giving the key intermediate furanone **8** in 86.0% yield. It was discovered that the reaction temperature was critical for such an alkylation, especially when adding **7**. The temperature had to be kept below −70 °C to prevent the formation of unwanted byproducts. Next, the furanone part of **8** was modified. Reduction with an excess of diisobutylaluminum hydride[16] followed by hydrolysis with aqueous hydrochloric acid generated the desired furan entity and simultaneously liberated the alcohol function by furnishing **9** in 86.2% yield.

Conversion of **9** to the final guanidine group via the corresponding amine did not proceed as originally planned. Usually, an allylic alcohol is converted into its azide and then reduced to the primary amine.[17] The standard practice

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* To whom correspondence should be addressed. Tel: +41-22-776-3693. Fax: +41-22-776-3601. E-mail: Charles.Jefford@chiorg.unige.ch.

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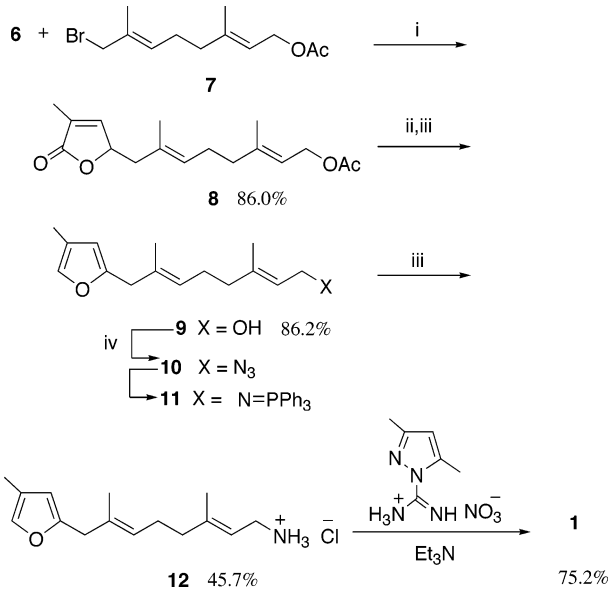
Scheme 3[a]



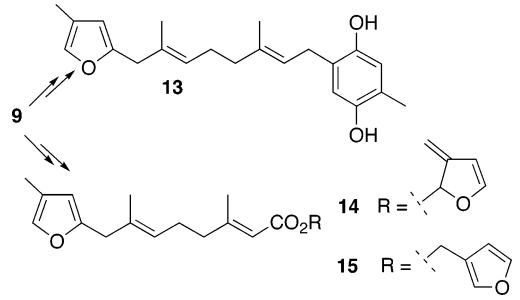
[a] (i) $AgOCOCF_3$; (ii) DIBAH; (iii) 1 M HCl; (iv) HN_3, $2Ph_3P$, DIPAD.

is catalytic hydrogenation over Lindlar catalyst[18] or reduction with zinc powder.[19] However, when the allylic azide **10** was treated with Lindlar catalyst under 1 atm of hydrogen, IR and ^1H NMR analyses of the resulting product indicated that the azide group underwent hydrogenation as expected, but that the adjacent allylic double bond had been reduced as well. Disappointingly, treatment of **10** with zinc powder in aqueous hydrochloric acid led to a similar result, namely, concomitant reduction of the azide group and furan ring.

Apart from preventing over-reduction, another prerequisite for preparing allylamines is control of regioselectivity. Allylic azides are liable to rearrange.[20,21] Consequently, reduction might give both allylic amines. A way of avoiding this possibility is to convert the azide to the iminophosphorane, the so-called Staudinger intermediate,[22] by reaction with triphenylphosphine. Such a procedure has been used to advantage for converting bromides[23] and alcohols[24] to amines. In the present instance, submission of **9** to the Mitsunobu reaction,[25] namely, treatment with hydrazoic acid in the presence of diisopropyl azodicarboxylate (DIPAD) and a 2-fold excess of triphenylphoshine,[26] was entirely successful (Scheme 3). Initially, the azide **10** was formed. The surplus PPh_3 in situ then produced, after expulsion of nitrogen, the nonisolated Staudinger intermediate **11**, which on hydrolysis with aqueous hydrochloric acid delivered the amine hydrochloride **12** in 45.7% yield. None of the allylically rearranged amine was observed, thereby indicating that only the terminal azide **10**, and not its sterically hindered allylic isomer, had undergone reaction with PPh_3. Finally, reaction of **12** with 3,5-dimethylpyrazole-l-carboxamidine nitrate[27] in the presence of triethylamine converted the amino to the guanidine group, thereby providing siphonodictidine (**1**) in 75.2% yield. The sample of synthetic **1** so obtained exhibited spectral data (^1H and ^{13}C NMR and MS) in complete agreement with those reported for the naturally occurring substance.[1]

In conclusion, the present synthetic route to **1** is operationally simple, requiring only seven steps to assemble the product from commonly available starting materials. Moreover, the synthesis is practical, giving **1** in 27.5% yield from **6**. It also demonstrates that 2-(*tert*-butyldimethylsiloxy)-3-methylfuran is an ideal reagent for preparing terpenes bearing the 4-methyl-2-furyl entity. It should be noted that

Scheme 4



alcohol **9** is a versatile intermediate that could be used for preparing other related furanosesquiterpenes. For example, the hydroquinone **13**, isolated from the Australian soft coral *Sinularia lochmodes*,[28] and marislin (**14**), found in *Chromodoris marislae*,[2] should be equally accessible by appropriate modification of the terminal hydroxyl group (Scheme 4). The present route to **9** also constitutes a formal synthesis of pleraplysillin-2 (**15**), a metabolite of the Mediterranean sponge *Pleraplysilla spinifera*,[29] since the final steps have already been described.[3]

Experimental Section

General Experimental Procedures. Melting points (uncorrected) were determined on a Reichert hot stage microscope. Infrared spectra (IR): Perkin-Elmer-681 spectrometer or FT-M Polaris, as solutions in a KBr cell. ^1H NMR: Varian XL-200 (200 MHz) and Bruker-AMX-400 (400 MHz) spectrometers; ^{13}C NMR: Varian XL-200 (50 MHz) or Bruker AMX-400 (100 MHz); chemical shifts (δ) are in ppm with reference to TMS (=0.00 ppm) as internal standard. Finnigan GC/MS-4023 instrument with the INCOS data system; electron impact, 70 eV. High-resolution MS: VG-7070E (resolution 5000−7000). Elemental analyses were performed by H. Eder, Service de Microchimie, Department of Pharmaceutical Chemistry, University of Geneva. All solvents were distilled prior to use. THF and Et_2O were dried over Na−K alloy/benzophenone and freshly distilled before use. CH_2C1_2 was dried over $NaHCO_3$, distilled, and stored over molecular sieves (Union Carbide Type 4 Å). HMPA was distilled from CaH_2 and stored over molecular sieves (Union Carbide Type 4 Å). Anhydrous EtOH was distilled from Mg turnings and a small amount of iodine. TLC was performed on plastic precoated silica gel 60 F_{254} plates (Merck, layer thickness 0.20 mm). Column chromatography (CC) (flash):[30] Merck silica gel 60 (230−400 mesh). α-Methylene-γ-butyrolactone was purchased from Fluka Chemie Sarl, 9471 Buchs, SG, Switzerland.

3-Methyl-2(5*H*)-furanone (5). Procedure l: A mixture of α-methylene-γ-butyrolactone (**4**) (5.60 g, 57.1 mmol) and $RhC1_3$·aq (0.27 g, 1.14 mmol) in absolute EtOH (3 mL) was heated at 100 °C in a sealed tube for 3 h under an atmosphere of N_2. The solvent was evaporated and the residue chromatographed on a column (SiO_2, Et_2O−pentane, 3:1) to give **5** (4.40 g, 78.46%, R_f = 0.34) and ethyl (*E*)-2-methylbut-2-enate (0.89 g, 12.2%, R_f = 0.87). Procedure-2: $RhC1_3$·aq (0.27 g, 1.14 mmol) was placed in a 50 mL round-bottomed flask. The flask was sealed with a rubber stopper, connected to a vacuum line (0.2 mmHg), pumped dry, and then filled with Ar. This procedure was repeated three times. To the flask was added **4** (5.60 g, 57.1 mmol) and absolute EtOH (3 mL) by syringe. The mixture was heated with stirring at 100 °C for 3 h. The workup according to procedure l gave ethyl (*E*)-2-methylbut-2-enate (0.50 g, 6.84%) and **5** (4.85 g, 86.6%): IR ($CHC1_3$) ν_{max} 3630, 3500, 3020, 2930, 2870, 1750, 1660, 1450, 1380, 1345, 1210, 1085, 1055, 825 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.14 (1H, m), 4.75 (2H, m), 1.92 (3H, m); LREIMS *m/z* 98 $[M]^+$ (71), 69 $[M - CHO]^+$ (100), 53 (8.3), 50 (8.3).

2-(*tert*-Butyldimethylsiloxy)-3-methylfuran (6). To a stirred solution of **5** (4.00 g, 40.8 mmol) and Et_3N (5.34 g, 53.0

mmol) in dry Et_2O (30 mL) was added *tert*-butyldimethylsilyl triflate (12.9 g, 48.9 mmol) under N_2 at 0 °C. The reaction mixture was stirred at 0 °C for 3 h until no starting material was left (as monitored by ^1H NMR). After separation of the Et_2O layer, the residue was extracted with Et_2O (30 mL). The combined Et_2O solutions were washed with cold aqueous saturated $NaHCO_3$ solution (2 × 20 mL), the solvent was evaporated, and the residue was distilled under reduced pressure to give a colorless oil (**6**) (78−80 °C/10 mmHg, 7.14 g, 88.5%): ^1H NMR ($CDC1_3$) δ 6.73 (1H, d, J = 2.5 Hz), 6.07 (1H, d, J = 2.5 Hz), 1.83 (3H, s), 0.99 (9H, s), 0.23 (6H, s); ^{13}C NMR ($CDCl_3$) δ 152.8 (qC), 131.1 (CH), 113.5 (CH), 92.1 (qC), 25.7 (CH_3), 25.4 (CH_3), 17.9 (qC), −4.6 (CH_3); *anal*. calcd for $C_{11}H_{20}O_2Si$ (212.37), C 62.13%, H 9.76%, found C 62.21%, H 9.94%.

[2*E*,6*E*]-8-Acetoxy-2,6-dimethyl-2,6-octadienyl bromide (7). The bromide **7** was prepared from geranyl acetate.[14]

[2′*E*,6′*E*]-5-[8′-Acetoxy-2′,6′-dimethylocta-2′,6′-dienyl]-3-methyI-2(5*H*)-furanone (8). To a stirred suspension of silver trifluoroacetate (2.2 g, 10 mmol) in dry CH_2C1_2 (20 mL) under Ar at −78 °C first was added **6** (1.88 g, 0.94 mmol) and then slowly dropwise a solution of **7** (2.5 g, 0.90 mmol) in CH_2C1_2 (2 mL). The stirred reaction mixture was gradually allowed to warm to 10 °C over 4 h, filtered through Celite, and washed with Et_2O (4 × 20 mL). The Et_2O solution was washed with H_2O (20 mL), aqueous saturated $NaHCO_3$ solution (20 mL), H_2O (20 mL), and brine (30 mL) and dried ($MgSO_4$). The solvent was evaporated under reduced pressure and the residual oil purified by CC (SiO_2, R_f = 0.25, Et_2O−pentane, 3:4) to give **8** (2.3 g, 86.0%) as a light yellow oil: IR ($CHC1_3$) ν_{max} 3020, 2980, 2930, 2860, 1750, 1449, 1378, 1360, 1232, 1100, 1060, 1020 cm^{-1}; ^1H NMR ($CDC1_3$) δ 7.02 (1H, quintet, J = 1.6 Hz), 5.32 (1H, br t, J = 7.0 Hz), 5.20 (1H, br t, J = 7.0 Hz), 4.94 (1H, tt, J = 7.2 Hz), 4.56 (1H, d, J = 7.0 Hz), 2.17−2.43 (2H, m), 2.04−2.16 (4H, m), 2.03 (3H, s), 1.89 (3H, t, J = 4.0 Hz), 1.68 (3H, s), 1.66 (3H, s); ^{13}C NMR ($CDC1_3$) δ 174.07 (qC), 170.95 (qC), 148.71 (CH), 141.61 (qC), 129.74 (qC), 129.70 (qC), 128.18 (CH), 118.50 (CH), 79.93 (CH), 61.22 (CH_2), 43.34 (CH_2), 39.01 (CH_2), 26.02 (CH_2), 20.94 (CH_3). 16.62 (CH_3), 16.31 (CH_3), 10.55 (CH_3); LREIMS *m*/*z* 292 $[M]^+$ (0), 249 $[M - CH_3CO]^+$ (1.30), 232 (0.81) 165 (0.93) 135 (21.87) 107 (30.71), 98 (34.18), 97 (100), 3 (60.08), 85 (23.51), 69 (35.93), 68 (44.74), 67 (39.24), 55 (31.54), 53 (32.39).

[2*E*,6*E*]-3,7-Dimethyl-8-(4′-methyl-2′-furanyl)-2,6-octadienol (9). To a stirred solution of **8** (672 mg, 2.3 mmol) in anhydrous THF (30 mL) was added dropwise a solution of DIBAH (9.2 mL, 1 M in THF, 9.2 mmol) under Ar at −78 °C. The mixture was stirred at −78 °C for 3 h, and aqueous HC1 (1 M, 45 mL) added dropwise with warming to −30 °C. The stirred reaction mixture was allowed to gradually warm to 5 °C over 2 h, poured into ice−water (100 mL), and extracted with Et_2O (4 × 30 mL). The Et_2O extracts were washed with H_2O (30 mL), aqueous saturated $NaHCO_3$ solution (30 mL), H_2O (30 mL), and brine (30 mL) and dried (Na_2SO_4). Evaporation of the solvent and chromatography of the residue (SiO_2, R_f = 0.20. Et_2O−pentane, 1:2) gave **9** (464 mg, 86.2%) as a colorless oil: IR ($CHC1_3$) ν_{max} 3620, 2530, 2860, 1445, 1388, 1115, 990, 900 cm^{-1}; ^1H NMR ($CDC1_3$) δ 7.06 (1H, quintet, J = 1.0 Hz), 5.87 (1H, s), 5.40 (1H, tm; J = 7.0 Hz), 5.20 (1H, tm, J = 7.0 Hz), 4.13 (2H, d, J = 7.0 Hz), 3.23 (2H, s), 2.13 (2H, m), 2.06 (2H, m), 1.98 (3H, d, J = 0.8 Hz), 1.67 (3H, s), 1.60 (3H, s); ^{13}C NMR ($CDCl_3$) δ 154.36 (qC), 139.31 (qC), 137.68 (CH), 132.13 (qC), 126.12 (CH), 123.72 (CH), 120.49 (qC), 108.77 (CH), 59.31 (CH_2), 39.23 (CH_2), 38.42 (CH_2), 26.31 (CH_2), 16.15 (CH_3), 15.85 (CH_3), 9.71 (CH_3); LREIMS *m*/*z* 234 $[M]^+$ (1.22), 216 $[M - 18]^+$ (9.50), 201 (2.91), 148 (38.85), 131 (59.25), 121 (35.49), 105 (49.80), 95 (74.17), 93 (90.9), 91(100), 81(28.06), 79 (64.42), 77 (62.14), 67 (57.24), 57 (39.86), 55 (78.05), 53 (68.07).

[2*E*,6*E*]-3,7-Dimethyl-8-(4′-methyl-2′-furanyl)-2,6-octadienyl Azide (10). To a stirred solution of **9** (250 mg, 1.07 mmol), HN_3 (1.10 mL, 1 M in benzene), and diisopropyl azodicarboxylate (234.8 mg, 1.2 mmol) in anhydrous THF (10 mL) was added a solution of PPh_3 (309.2 mg, 1.2 mmol) in THF (5 mL) under N_2 at 20−30 °C. The mixture was stirred at room temperature for a further 4 h. Evaporation of the solvent gave a residue, which on CC (SiO_2, R_f = 0.17, pentane−benzene, 6:1) gave **10** as a colorless oil (240 mg, 86.6%): IR ($CHC1_3$) ν_{max} 2980, 2930, 2880, 2105, 1550, 1448, 1255, 1115, 950, 873, 805 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.06 (1H, quintet, J = 1.0 Hz), 5.87 (1H, s), 5.33 (1H, tm, J = 7.0 Hz), 5.20 (1H, m), 3.76 (2H, d, J = 7.0 Hz), 3.22 (2H, s), 2.09−2.22 (4H, m), 1.98 (3H, d, J = 1.0 Hz), 1.70 (3H, s), 1.60 (3H, s).

Hydrogenation of 10. Method A: A solution of **10** (25.9 mg, 0.1 mmol) in EtOH (2 mL) was stirred with Lindlar catalyst (6.2 mg, 5% $Pd/CaCO_3$) under 1 atm of H_2 at room temperature until TLC analysis indicated that all **10** had reacted (about 5 h). The catalyst was removed by filtration. Evaporation of the solvent gave an oil (24 mg). ^1H NMR (60 MHz) analysis revealed that both the N_3 group and the allylic double bond had been hydrogenated. Method B: A mixture of **10** (25.9 mg, 0.1 mmol), Zn powder (26 mg, 0.4 mmol), and aqueous HCl (6 M, 2 mL) was stirred under N_2 at 80 °C until TLC analysis indicated that all the azide had reacted (2 h). The reaction mixture was washed with Et_2O (2 × 2 mL); the aqueous layer was treated with aqueous NaOH (3 N), extracted with CH_2Cl_2 (3 × 5 mL), and dried (K_2CO_3). Evaporation of the solvent gave an oil (20 mg). The IR spectrum of the resulting product showed that the peak at 2105 cm^{-1} characteristic of the N_3 group had disappeared. ^1H NMR (60 MHz) analysis also revealed hydrogenation of the furan ring.

[2*E*,6*E*]-3,7-Dimethyl-8-(4′-methyl-2′-furanyl)-2,6-octadienylamine (12). To a stirred solution of **9** (247 mg, 1.06 mmol) in anhydrous THF (10 mL) was added a solution of HN_3 (1.2 mL, 1 M in benzene, 1.2 mmol), followed by a solution of diisopropyl azodicarboxylate (247 mg, 95%, 1.1 mmol) in THF (2 mL). To the resulting mixture was slowly added dropwise a solution of PPh_3 (630 mg, 2.32 mmol) in THF (5 mL) at 20−30 °C. After stirring at room temperature for 2 h and heating the mixture under reflux for 6 h, H_2O (2 mL) was added followed by heating for another 3 h. The solvent was evaporated under reduced pressure and the residue partitioned between CH_2C1_2 (15 mL) and aqueous HC1 (1 M, 15 mL). The aqueous layer was extracted with CH_2C1_2 (2 × 15 mL). The combined organic phases were washed with brine and dried ($MgSO_4$). Evaporation of the solvent gave a residue, which on purification by CC (SiO_2, CH_2C1_2−MeOH, 10:1) afforded a light yellow solid (130 mg, 45.7%). Crystallization gave the amine hydrochloride **12** (THF−*n*-hexane, 1:1): mp 132−134 °C; IR ($CHC1_3$) ν_{max} 2930, 2870, 1440, 1380, 1260, 1110, 1020, 940, 860, 800 cm^{-1}; ^1H NMR ($CDC1_3$) δ 8.28 (2H, br s), 7.06 (1H, s), 5.85 (1H, s), 5.34 (1H, br t, J = 7.0 Hz), 5.18 (1H, m), 3.55 (2H, br d, J = 7.0 Hz), 3.21 (2H, s), 2.08 (4H, m), 1.97 (3H, s), 1.71 (3H, s), 1.57 (3H, s); ^{13}C NMR ($CDCl_3$) δ 154.17 (qC), 144.64 (qC), 137.65 (CH), 132.39 (qC), 125.65 (CH), 120.41 (qC), 115.23 (CH), 108.76 (CH), 39.30 (CH_2), 38.37 (CH_2), 37.28 (CH_2), 26.28 (CH_2), 16.61 (CH_3), 15.85 (CH_3), 9.76 (CH_3); HREIMS *m*/*z* 233.1782 (calcd for $C_{15}H_{23}NO$, 233.1786).

[2*E*,6*E*]-3,7-Dimethyl-8-(4′methyl-2′-furanyl)-2,6-octadienylguanidine (Registry Number 88316-91-0) (Siphonodictidine (1)). To a stirred solution of 3,5-dimethylpyrazole-l-carboxamidine nitrate (55.3 mg, 0.27 mmol) and **12** (64 mg, 0.24 mmol) in EtOH (3 mL) was added Et_3N to bring the pH to 9−10. The reaction mixture was heated under reflux for 6 h under an Ar atmosphere. The solvent was evaporated under reduced pressure, and the residue extracted with dry Et_2O (3 × 2 mL) to remove 3,5-dimethylpyrazole and unreacted **12**. To remove Et_3NHNO_3, the crude product was treated with an aqueous solution of NaOH (1 M, 10 mL), extracted with CH_2C1_2 (3 × 15 mL), and dried ($MgSO_4$). Evaporation of the solvent gave a residue, which on purification by CC (SiO_2, CH_2C1_2−MeOH, 10:1) (TLC, R_f = 0.37, CH_2C1_2−MeOH, 4:1) gave **1** (49 mg, 75.2%): IR ($CHC1_3$) ν_{max} 3060, 1630, 1620, 1590 cm^{-1}; ^1H NMR ($CDC1_3$) δ 7.80 (1H, br s), 7.06 (1H, s), 5.86 (1H, s), 5.18 (2H, m), 3.76 (2H, d, J = 6.0 Hz), 3.22 (2H, s), 2.00−2.20 (4H, m), 1.97 (3H, s), 1.68 (3H, s), 1.58 (3H, s); ^{13}C NMR ($CDC1_3$) δ 158.02 (qC), 154.25 (qC), 141.62 (qC), 137.72 (CH), 132.57 (qC), 125.72 (CH), 120.54 (qC), 118.22 (CH), 108.89 (CH), 39.67 (CH_2), 39.18 (CH_2), 38.42 (CH_2), 26.34 (CH_2), 16.48 (CH_3), 15.92 (CH_3), 9.75 (CH_3); HREIMS *m*/*z* 275

$[M]^+$ (3.2), 216 $[M - guanyl]^+$ (2.4), 148.0874 (22.6) (calcd for $C_{10}H_{12}O$, 148.0888), 126.1035 (100) (calcd for $C_6H_{12}N_3$, 126.1031), 105 (10.4), 84 (27.4), 60 $[guanyl + H]^+$ (16.9).

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