Metabolites of the Sponge *Strongylophora durissima* from Maricabán Island, Philippines

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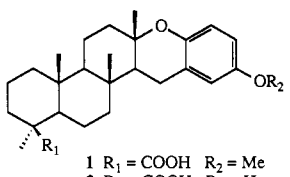
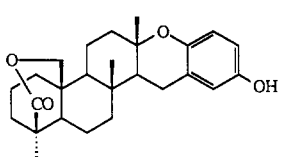
The sponge *Strongylophora durissima* from the Philippines contains the known meroditerpenoids strongylophorine-2 (**2**) and strongylophorine-3 (**3**), three new meroditerpenoids, strongylophorines-4, -5, and -8 (**4**, **5**, and **8**, respectively), and two novel enediones, strongylophorine-6 (**6**) and strongylophorine-7 (**7**). It is proposed that the nonaromatic compounds strongylophorines-6 and -7 (**6** and **7**) were derived by cyclization of a quinone **9**, which might be obtained by oxidation of hydroquinone **8**. The structures of the new strongylophorines **4**–**8** were elucidated by interpretation of spectral data and chemical interconversions. The strongylophorines show mild activity against Gram-positive bacteria.

In 1978, Braekman and co-workers[1] reported the isolation and characterization of three ichthyotoxic meroditerpenoids called strongylophorines-1, -2, and -3 (**1**, **2**, and **3**) from the sponge *Strongylophora durissima* collected near Laing Island (Papua, New Guinea). Similar ichthyotoxic and cytotoxic meroditerpenoids were isolated from the brown algae *Stypopodium zonale*[2,3] and *Taonia atomaria*.[4] In the course of studying pharmacologically active metabolites from sponges, we obtained a specimen of *S. durissima*[5] from Maricabán Island, Philippines. This specimen contained the known compounds strongylophorines-2 and -3 (**2** and **3**), together with five new strongylophorines (**4**–**8**). In two of the new compounds, strongylophorines-6 and -7 (**6** and **7**), the aromatic ring has been replaced by a cyclohexene-3,6-dione ring system, which represents an unusual loss of aromaticity.



1 R_1 = COOH R_2 = Me
3 R_1 = COOH R_2 = H
4 R_1 = CHO R_2 = H
5 R_1 = CH_2OH R_2 = H



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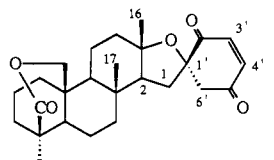

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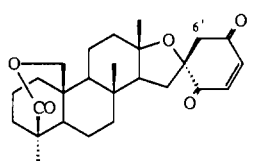

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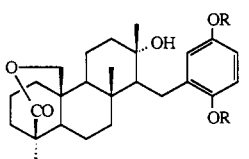

8 R = H
11 R = Ac

Unlike the specimen of *S. durissima* from Laing Island which was sun-dried, our specimen was placed in methanol immediately after collection. This milder treatment, together with the use of a more polar extraction solvent, enabled the isolation of both the less stable and the more polar strongylophorines (**4**–**8**) together with two of the known metabolites. Chromatography of the methanol-soluble material on silica gel followed by final purification using HPLC allowed isolation of the following compounds (in order of polarity): strongylophorine-4 (**4**, 0.02% dry wt), strongylophorine-5 (**5**, 0.01% dry wt), strongylophorine-3 (**3**, 0.1% dry wt), strongylophorine-2 (**2**, 0.06% dry wt), strongylophorine-6 (**6**, 0.024% dry wt), strongylophorine-7 (**7**, 0.02% dry wt), and strongylophorine-8 (**8**, 0.06% dry wt). Strongylophorines-2 and -3 (**2** and **3**) were identified by comparison of spectral data with the literature values.[1]

Strongylophorine-4 (**4**) was obtained as colorless crystals, mp 196–198 °C, from hexane/ethyl acetate. The molecular formula, $C_{26}H_{36}O_3$, was obtained from the high-resolution mass measurement. The presence of an aldehyde group was indicated by the infrared signals at 2845 and 1715 cm^{-1}, the ^1H NMR signal at δ 9.82 (s, 1 H), and the ^{13}C NMR signal at δ 206 (d). Comparison of the ^1H and ^{13}C NMR spectra of aldehyde **4** with those of strongylophorine-3 (**3**) indicated that the two compounds had the same carbon skeleton and stereochemistry.

The corresponding alcohol, strongylophorine-5 (**5**), was obtained as an oil. The molecular formula, $C_{26}H_{38}O_3$, was obtained by high-resolution mass measurement and was compatible with the alcohol **5** being the primary alcohol that would arise by reduction of aldehyde **4**. The infrared spectrum contained a band at 3340 cm^{-1} due to the phenolic and hydroxyl groups. The ^1H NMR spectrum contained three signals at δ 6.62 (d, 1 H, J = 9 Hz), 6.56 (d, 1 H, J = 9 Hz), and 6.54 (s, 1 H), that were assigned to the 1,2,4-trisubstituted aromatic ring, and at 4.05 (d, 1 H, J = 11.9 Hz) and 3.92 (d, 1 H, J = 11.9 Hz) due to a primary alcohol adjacent to a fully substituted carbon atom. Both the known compound strongylophorine-3 (**3**) and strongylophorine-4 (**4**) were converted into strongylophorine-5 (**5**) by lithium aluminum hydride reduction to confirm the proposed structural assignments.

Strongylophorine-6 (**6**) was obtained as colorless crystals, mp 243–244 °C dec, from diethyl ether. The molecular formula, $C_{26}H_{34}O_5$, was obtained from the high-resolution mass measurement. The molecular formula required 10 units of unsaturation yet the ultraviolet absorption at 223

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(1) Braekman, J. C.; Daloze, D.; Hulot, G.; Tursch, B.; Declercq, J. P.; Germain, G.; Van Meerssche, M. *Bull. Soc. Chim. Belg.* **1978**, *87*, 917.
(2) Gerwick, W. H.; Fenical, W.; Fritsch, N.; Clardy, J. *Tetrahedron Lett.* **1979**, *145*.
(3) Gerwick, W. H.; Fenical, W. *J. Org. Chem.* **1981**, *46*, 22.
(4) González, A. G.; Darias, J.; Martín, J. D. *Tetrahedron Lett.* **1971**, 2729. González, A. G.; Darias, J.; Martín, J. D.; Pascual, C. *Tetrahedron* **1973**, *29*, 1605.
(5) The sponge was identified by Mary Kay Harper as a species of *Strongylophora* that fits the description of *S. durissima* but the sponge has not been compared with authentic material; Scripps Institution of Oceanography Benthic Invertebrate Collection Catalog no. P1100.

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nm (ε 11 800) clearly indicated that the aromatic ring of the known strongylophorines could not be present. Comparison of spectral data strongly suggested that the diterpene portion of strongylophorine-6 (**6**) was identical with that of strongylophorine-2 (**2**), the structure of which had been determined by X-ray analysis of the corresponding monoacetate.[1] The presence of the lactone ring was indicated by the infrared band at 1720 cm^{-1}, the ^1H NMR signals at δ 4.75 (d, 1 H, J = 12.2 Hz) and 4.02 (d, 1 H, J = 12.2 Hz), and the ^{13}C NMR signals at δ 176.5 (s) and 73.0 (t). The structure of the enedione portion of strongylophorine-6 (**6**) was elucidated by assuming that it had been formed by modification of an aromatic ring. The ^{13}C NMR spectrum contains two unsaturated carbonyl signals at δ 196.6 (s) and 195.8 (s), two olefinic signals at 140.8 (d) and 140.5 (d), two carbons bearing oxygen at 83.9 (s) and 83.8 (s), and one more aliphatic methylene carbon signal than is present in strongylophorine-2. Since one of the carbons bearing oxygen must be assigned to C-3, the other signal at δ 83–84 must be assigned to a spiro-carbon bearing the same oxygen. Two possible ring systems emerge: one, as assigned, with a tetrahydrofuran ring fused to a cyclohexenedione ring, or the alternative, with a tetrahydropyran ring fused to a cyclopentenedione ring. The latter possibility is eliminated by the ^1H NMR spectrum that contains methylene signals at δ 2.98 (d, 1 H, J = 15.8 Hz) and 2.87 (d, 1 H, J = 15.8 Hz) that were not coupled to any other signals and must therefore be assigned to CH_2-6′. Decoupling difference spectroscopy was employed to locate the signals at δ 1.61 (dd, 1 H, J = 13.7, 7.6 Hz, H-1α) and 1.49 (dd, 1 H, J = 11.5, 7.6 Hz, H-2) that were coupled to the signal at 2.45 (dd, 1 H, J = 13.7, 11.5 Hz, H-1β). The signals for H-3′ (δ 6.87) and H-4′ (δ 6.70) were assigned on the basis of the coupling of the H-4′ signal with the H-6′ signals.

The stereochemistry of strongylophorine-6 (**6**) was determined by using NOEDS experiments. The geometry of the 2,3-ring junction is defined by the nuclear Overhauser enhancements recorded between H-1β and the C-16 (3%) and C-17 (2%) methyl groups. The observation of a small nuclear Overhauser enhancement (2%) of H-2 on irradiation of H-6′α defined the geometry at C-1′, the spiro-carbon atom. In addition, the chemical shifts of H-1β (δ 2.45) and H-1α (δ 1.61) require the 2′-carbonyl group to be on the β face of the tetrahydrofuran ring.

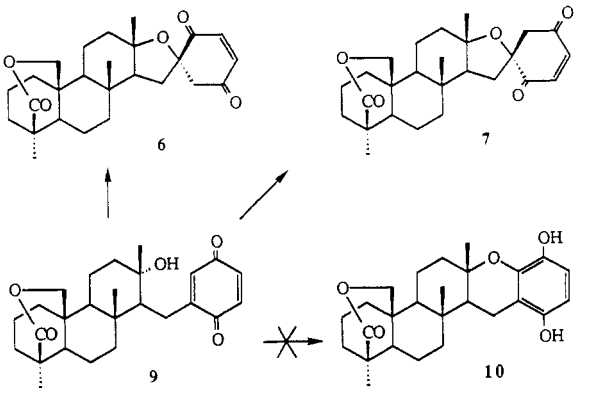
Strongylophorine-7 (**7**) was obtained as colorless needles, mp 237–238 °C dec, from ether. Comparison of the spectral data of strongylophorines-6 and -7 (**6** and **7**) revealed very few differences and suggested that the compounds were isomeric at C-1′. The NOEDS data supported this hypothesis; irradiation at the C-16 methyl signal at δ 1.22 caused a 5% enhancement of the C-17 methyl signal at δ 0.97, a 7% enhancement of the H-6′β signal at δ 3.13, and a 2.5% enhancement of the H-6′α signal at δ 2.99. In addition, the H-1α signal at δ 2.28 (dd, 1 H, J = 10.2, 4.1 Hz) was shifted downfield by the C-2′ carbonyl group.

The two enediones **6** and **7** can be formed by a 5-*exo-trig* cyclization of an intermediate quinone **9** (see Scheme I). The alternative 6-*endo-trig* cyclization, permitted under Baldwin's Rules,[6] would give rise to a more stable aromatic compound **10**, which was not found among the metabolites of *S. durissima*. However, the hydroquinone corresponding to quinone **9** was isolated as the most polar of the metabolites, strongylophorine-8 (**8**).

Strongylophorine-8 (**8**), mp 246–247 °C, was crystallized from methanol. The molecular formula, $C_{26}H_{36}O_5$, was

(6) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.

Scheme I. A Proposed Mechanism for the Synthesis of Strongylophorines-6 and -7 (6 and 7)



obtained from a chemical ionization high-resolution mass measurement of the (M + 1) ion. The infrared spectrum contained a lactone carbonyl band at 1710 cm^{-1} and a strong hydroxyl band centered at 3320 cm^{-1}. The ultraviolet absorption at 295 nm is typical of a hydroquinone. Because of the general insolubility of the hydroquinone **8** in NMR solvents, better data were recorded for the corresponding diacetate **11**, which was prepared by reaction of **8** with acetic anhydride in pyridine. The presence of a 2-substituted hydroquinone diacetate ring system in **11** was indicated by ^1H NMR signals at δ 7.00 (d, 1 H, J = 9 Hz), 6.98 (br s, 1 H), 6.91 (br d, 1 H, J = 9 Hz), 2.34 (s, 3 H), and 2.29 (s, 3 H) and by ^{13}C NMR signals at δ 169.4 (2 s), 148.2 (s), 145.6 (s), 137.3 (s), 123.4 (d), 123.2 (d), 119.7 (d), 21.1 (q), and 21.2 (q). The tertiary alcohol bearing a methyl group at C-3 gave rise to a ^{13}C NMR signal at 73.3 (s) and a ^1H NMR signal at δ 1.24 (s, 3 H). The structure of the hydroquinone **8** was confirmed by its conversion into strongylophorine-2 (**2**) on treatment with *p*-toluenesulfonic acid in refluxing benzene for 30 min. The similarity of chemical shifts for the three methyl signals in **2** and **8** indicates an axial methyl group at C-3 of strongylophorine-8 (**8**).

Using the standard paper disk assay procedure, the strongylophorines exhibited mild antimicrobial activity against *Bacillus subtilis* and *Staphylococcus aureus* with the two diones **6** and **7** showing the greatest inhibition.

Experimental Section

A specimen of *S. durissima* (50 g dry wt) was collected by hand using SCUBA at Maricabán Island, Philippines, and was stored in methanol. After 3 months at 4 °C, the methanol was decanted and the sponge was washed with fresh methanol. The combined methanol extracts were evaporated to give an aqueous residue to which water (200 mL) was added. The aqueous suspension was extracted with hexane (2 × 200 mL) and ethyl acetate (2 × 200 mL). The extracts were dried, and the solvents were evaporated to obtain oils (hexane, 50 mg, 0.1% dry wt; ethyl acetate, 700 mg, 1.4% dry wt). The ethyl acetate soluble fraction was chromatographed on silica gel (200 g) using solvents of increasing polarity from hexane to ethyl acetate. Selected fractions were subjected to HPLC on Partisil to obtain, in order of polarity, strongylophorine-4 (**4**, 0.02% dry wt), strongylophorine-5 (**5**, 5 mg 0.001% dry wt), strongylophorine-3 (**3**, 50 mg, 0.1% dry wt), strongylophorine-2 (**2**, 30 mg, 0.06% dry wt), strongylophorine-6 (**6**, 12 mg, 0.024% dry wt), strongylophorine-7 (**7**, 10 mg, 0.02% dry wt), and strongylophorine-8 (**8**, 30 mg, 0.06% dry wt).

Strongylophorine-2 (2): eluted from Partisil with 5% methanol in dichloromethane; IR, UV, and ^1H NMR (pyridine-d_5) spectra identical with literature values;[1] ^1H NMR ($CDCl_3$) δ 6.62 (d, 1 H, J = 9 Hz), 6.57 (d, 1 H, J = 9 Hz), 6.56 (s, 1 H), 4.78 (dd, 1 H, J = 13, 2 Hz), 4.03 (d, 1 H, J = 13 Hz), 2.59 (d, 1 H, J = 12 Hz), 2.58 (d, 1 H, J = 7 Hz), 2.18 (d, 1 H, J = 12 Hz), 1.21 (s, 3 H), 1.17 (s, 3 H), 1.00 (s, 3 H); ^{13}C NMR (pyridine-d_5) 176.0 (s),

152.1 (s), 146.5 (s), 123.0 (s), 117.9 (d), 116.7 (d), 115.3 (d), 76.0 (s), 73.4 (t), 55.2 (d), 52.8 (d), 50.0 (d), 43.2 (s), 41.8 (t), 40.3 (t), 39.8 (t), 38.0 (t), 36.6 (s), 36.5 (s), 23.5 (q), 22.6 (t), 21.0 (t), 21.0 (q), 20.5 (t), 18.6 (t), 15.5 (q); mass spectrum, *m/z* (intensity) 410 (98), 287 (100), 259 (9), 229 (96).

Strongylophorine-3 (3): eluted from Partisil with 40% ethyl acetate in hexane; IR, UV, and ^{1}H NMR (pyridine-d_5) spectra identical with literature values;[1] ^{1}H NMR ($CDCl_3$) δ 6.62 (d, 1 H, J = 8.6 Hz), 6.58 (s, 1 H), 6.57 (d, 1 H, J = 8.6 Hz), 2.56 (d, 1 H, J = 9 Hz), 2.15 (d, 1 H, J = 11.8 H), 1.25 (s, 3 H), 1.22 (s, 3 H), 0.97 (s, 3 H), 0.82 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 178.8 (s), 151.1 (s), 147.1 (s), 123.6 (s), 117.9 (d), 116.3 (d), 114.8 (d), 76.3 (s), 60.8 (d), 57.3 (d), 53.4 (d), 43.7 (s), 42.0 (t), 41.4 (t), 40.8 (t), 38.8 (t), 38.6 (s), 37.6 (s), 29.0 (q), 22.9 (t), 20.9 (q), 20.5 (t), 19.9 (t), 19.3 (t), 15.9 (q), 14.7 (q); mass spectrum, *m/z* (intensity) 412 (100), 395 (1), 367 (2), 289 (90).

Strongylophorine-4 (4): eluted from Partisil with 20% ethyl acetate in hexane; mp 196–198 °C; $[\alpha]_D$ −55° (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) 3350, 2845, 1715, 1495 cm^{-1}; UV (MeOH) 295 nm (ϵ 1300), (MeOH + NaOH) 303 nm; ^{1}H NMR ($CDCl_3$) δ 9.82 (s, 1 H), 6.63 (d, 1 H, J = 8 Hz), 6.57 (d, 1 H, J = 8 Hz), 6.56 (s, 1 H), 2.57 (d, 2 H, J = 9.6 Hz), 1.16 (s, 3 H), 1.02 (s, 3 H), 0.91 (s, 3 H), 0.73 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 206 (d), 148.7 (s), 147.0 (s), 123.0 (s), 117.5 (d), 115.7 (d), 114.3 (d), 76.4 (s), 59.5 (d), 56.7 (d), 53.4 (s), 52.3 (d), 48.4 (s), 41.0 (t), 40.7 (t), 39.2 (t), 37.7 (s), 34.4 (t), 24.1 (q), 22.4 (t), 20.5 (q), 18.8 (t), 18.3 (t), 17.8 (t), 15.8 (q), 15.2 (q); mass spectrum, *m/z* (intensity) 368 (8), 367 (4); HRMS obsd *m/z* 396.2645, $C_{26}H_{36}O_3$ requires 396.2664.

Strongylophorine-5 (5): eluted from Partisil with 55% ether in heexane; oil; IR ($CHCl_3$) 3340, 1490, 1220, 1020 cm^{-1}; UV (MeOH) 296 nm (ϵ 2440), (MeOH + NaOH) 305 nm; ^{1}H NMR ($CDCl_3$) δ 6.62 (d, 1 H, J = 9 Hz), 6.56 (d, 1 H, J = 9 Hz), 6.54 (s, 1 H), 4.05 (d, 1 H, J = 11.9 Hz), 3.92 (d, 1 H, J = 11.9 Hz), 2.59 (br d, 1 H, J = 9.8 Hz), 2.21 (d, 1 H, J = 14 Hz), 1.17 (s, 3 H), 1.09 (s, 3 H), 0.88 (s, 3 H), 0.80 (s, 3 H); ^{13}C NMR ($CDCl_3$) 148.7 (s), 148.5 (s), 123.4 (s), 117.5 (d), 115.7 (d), 114.2 (d), 76.8 (s), 62.9 (t), 61.4 (d), 56.9 (d), 52.8 (d), 42.4 (s), 42.3 (t), 41.7 (t), 41.5 (s), 38.5 (s), 34.5 (t), 33.9 (t), 22.6 (q), 21.9 (t), 21.9 (q), 20.1 (t), 18.4 (t), 18.4 (q), 18.0 (t), 15.5 (q); mass spectrum, *m/z* (intensity) 398 (60), 380 (18), 275 (30), 257 (42); HRMS obsd *m/z* 398.2798, $C_{26}H_{38}O_3$ requires 398.2821.

Strongylophorine-6 (6): eluted from Partisil with 40% ethyl acetate in hexane; mp 243–244 °C dec; $[\alpha]_D$ −47.1° (*c* 0.42, $CHCl_3$); IR ($CHCl_3$) 1720 cm^{-1}; UV (MeOH) 223 nm (ϵ 11 800); ^{1}H NMR ($CDCl_3$) δ 6.87 (d, 1 H, J = 10.5 Hz), 6.70 (d, 1 H, J = 10.5 Hz), 4.75 (dd, 1 H, J = 12, 2 Hz), 4.02 (d, 1 H, J = 12.2 Hz), 2.98 (d, 1 H, J = 15.8 Hz), 2.87 (d, 1 H, J = 15.8 Hz), 2.45 (dd, 1 H, J = 13.7, 11.5 Hz), 2.12 (d, 1 H, J = 12.2 Hz), 1.61 (dd, 1 H, J = 13.7, 7.6 Hz), 1.49 (dd, 1 H, J = 11.5, 7.6 Hz), 1.20 (s, 3 H), 1.10 (s, 3 H), 0.99 (s, 3 H); ^{13}C NMR ($CDCl_3$) 196.6 (s), 195.8 (s), 176.5 (s), 140.8 (d), 140.5 (d), 83.9 (s), 83.8 (s), 73.0 (t), 59.7 (d), 56.1 (d), 51.4 (t), 50.9 (d), 43.1 (s), 40.4 (t), 40.3 (t), 40.1 (t), 38.8 (t), 36.5 (s), 36.2 (s), 29.5 (t), 23.4 (q), 23.2 (q), 20.7 (t), 20.2 (t), 19.6 (t), 16.3 (q); mass spectrum, *m/z* (intensity) 426 (7), 287 (100), 229 (68); HRMS obsd *m/z* 426.2415, $C_{26}H_{34}O_5$ requires 426.2406.

Strongylophorine-7 (7): eluted from Partisil with 40% ethyl acetate in hexane; mp 237–238 °C dec; $[\alpha]_D$ −18.3° (*c* 3.3, $CHCl_3$); IR ($CHCl_3$) 1720 cm^{-1}; UV (MeOH) 224 nm (ϵ 12 700) ^{1}H NMR ($CDCl_3$) δ 6.81 (d, 1 H, J = 10.1 Hz), 6.72 (d, 1 H, J = 10.1 Hz), 4.73 (dd, 1 H, J = 12, 2 Hz), 4.01 (d, 1 H, J = 12 Hz), 3.13 (d, 1 H, J = 16.2 Hz), 2.99 (d, 1 H, J = 16.2 Hz), 2.28 (dd, 1 H, J = 10.2, 4.1 Hz), 1.22 (s, 3 H), 1.19 (s, 3 H), 0.97 (s, 3 H); ^{13}C NMR ($CDCl_3$) 195.8 (s), 195.5 (s), 176.5 (s), 140.9 (d), 140.1 (d), 83.7 (s), 83.4 (s), 73.1 (t), 59.2 (d), 55.8 (d), 51.9 (t), 50.8 (d), 43.2 (s), 40.2 (t), 40.1 (t), 39.9 (t), 38.7 (t), 36.6 (s), 36.1 (s), 30.8 (t), 24.5 (q), 23.2 (q), 20.7 (t), 20.2 (t), 19.5 (t), 16.3 (q); MS *m/z* (intensity) 426 (8), 287 (100), 229 (75); HRMS obsd *m/z* 426.2398, $C_{26}H_{34}O_5$ requires 426.2406.

Strongylophorine-8 (8): eluted from Partisil with 1:1 ethyl acetate/hexane; mp 246–247 °C; $[\alpha]_D$ −9.1° (*c* 0.55, acetone); IR ($CHCl_3$) 3320, 1710, 1210, 1150 cm^{-1}; UV (MeOH) 295 nm (ϵ 9340), (MeOH + NaOH) 312 nm; ^{1}H NMR (pyridine-d_5) δ 7.31 (d, 1 H, J = 2.5 Hz), 7.16 (d, 1 H, J = 8.6 Hz), 7.09 (dd, 1 H, J = 8.6, 2.5 Hz), 4.70 (dd, 1 H, J = 12.2, 1.5 Hz), 3.96 (d, 1 H, J = 12.2 Hz), 3.23 (br d, 1 H, J = 16 Hz), 2.65 (dd, 1 H, J = 16, 5 Hz), 1.39 (s, 3 H), 1.18 (s, 3 H), 0.94 (s, 3 H); ^{13}C NMR ($CDCl_3$ + acetone-d_6) 176.1 (s), 148.6 (s), 148.2 (s), 129.2 (s), 117.7 (d), 116.4 (d), 113.4 (d), 73.8 (s), 72.9 (t), 60.8 (d), 54.6 (d), 49.5 (d), 43.2 (t), 42.6 (s), 39.6 (t), 39.5 (t), 38.8 (s), 38.7 (t), 36.1 (t), 26.6 (t), 23.9 (q), 22.5 (q), 20.3 (t), 19.5 (t), 18.7 (t), 15.9 (q); MS *m/z* (intensity) 410 (52), 287 (100), 229 (82); CIHRMS obsd *m/z* 429.2661, $C_{26}H_{37}O_5$ (M + 1) requires 429.2641.

Reduction of Strongylophorine-4 (4) to Strongylophorine-5 (5). Lithium aluminum hydride (2 mg) was added to a solution of strongylophorine-4 (**4**, 2 mg) in dry ether (1 mL), and the resulting suspension was stirred at 25 °C for 1 h. Excess reagent was destroyed by careful addition of water, and the product was partitioned between ether (3 × 5 mL) and water (5 mL). The combined ether extracts were dried over anhydrous sodium sulfate, and the solvent was evaporated. The residue was filtered through a small silica gel column using 25% ethyl acetate in hexane to obtain strongylophorine-5 (**5**, 1.2 mg).

Reduction of Strongylophorine-3 (3) to Strongylophorine-5 (5). A solution of diazomethane in ether (3 drops) was added to strongylophorine-3 (**3**, 5 mg) in ether (1 mL), and the pale yellow solution was maintained at 25 °C for 1 h. The reaction mixture was diluted with ether (to 10 mL) and washed, first with 0.1 N hydrochloric acid (10 mL) and then with water (10 mL). The ethereal solution was dried over anhydrous sodium sulfate, and the solvent was evaporated to obtain a quantitative yield of the methyl ester of strongylophorine-3: ^{1}H NMR ($CDCl_3$) δ 6.62 (dd, 1 H, J = 8, 1.5 Hz), 6.58 (s, 1 H), 6.57 (d, 1 H, J = 8 Hz), 3.65 (s, 3 H), 2.57 (d, 1 H, J = 9 Hz), 2.17 (d, 1 H, J = 12 Hz), 1.18 (s, 3 H), 1.16 (s, 3 H), 0.90 (s, 3 H), 0.68 (s, 3 H). Lithium aluminum hydride (3 mg) was added to a solution of the methyl ester in dry ether (1 mL), and the resulting suspension was stirred for 3 h at 25 °C. The reaction mixture was worked up as described above to obtain strongylophorine-5 (**5**, 3 mg).

Acetylation of strongylophorine-8 (8). A solution of strongylophorine-8 (**8**, 5 mg) and acetic anhydride (3 drops) in dry pyridine (1 mL) was allowed to stand overnight at 25 °C. The product was poured into 0.1 M hydrochloric acid, and the organic material was extracted with chloroform. The organic extract was washed with water and dried over anhydrous sodium sulfate, and the solvent was evaporated to obtain an oil (5 mg). The crude reaction mixture was purified by LC on Partisil using 5% methanol in dichloromethane as eluant to obtain the diacetate **11** (3.5 mg, 59% yield): oil; ^{1}H NMR ($CDCl_3$) δ 7.00 (d, 1 H, J = 9 Hz), 6.98 (d, 1 H, J = 2 Hz), 6.91 (dd, 1 H, J = 9, 2 Hz), 4.72 (dd, 1 H, J = 12, 2 Hz), 3.98 (d, 1 H, J = 12 Hz), 2.72 (dd, 1 H, J = 15, 4 Hz), 2.55 (dd, 1 H, J = 15, 6 Hz), 2.34 (s, 3 H), 2.29 (s, 3 H), 2.14 (dd, J = 12, 2 Hz), 1.24 (s, 3 H), 1.16 (s, 3 H), 1.02 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 176.5 (s), 169.4 (2 s), 148.2 (s), 145.6 (s), 137.3 (s), 123.4 (d), 123.2 (d), 119.7 (d), 73.3 (s), 73.1 (t), 62.5 (d), 55.2 (d), 50.1 (d), 44.3 (s), 43.1 (s), 40.1 (2 t), 38.8 (2 t), 36.6 (s), 24.8 (t), 24.3 (q), 23.0 (q), 21.2 (q), 21.1 (q), 20.8 (t), 20.3 (t), 19.1 (t), 16.2 (q); mass spectrum, *m/z* (intensity) 512 (8), 494 (2), 470 (29), 428 (100), 287 (87).

Conversion of Strongylophorine-8 (8) into Strongylophorine-2 (2). A solution of strongylophorine-8 (**8**, 4 mg) in dry benzene (1 mL) containing *p*-toluenesulfonic acid (~0.5 mg) was refluxed for 30 min. The cooled solution was poured into chloroform (10 mL) and washed with water (5 mL). The organic extract was dried over anhydrous sodium sulfate, and the solvent was evaporated to obtain a crude product that was purified by LC on Partisil using 2% methanol in dichloromethane to obtain strongylophorine-2 (**2**, 3 mg, 78% yield).

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Registry No. **2**, 70214-92-5; **3**, 70214-93-6; **3** methyl ester, 70214-91-4; **4**, 125282-11-3; **5**, 125282-12-4; **6**, 125282-13-5; **7**, 125302-26-3; **8**, 125329-09-1; **8** 25-di-*O*-acetate, 125282-15-7; **9**, 125282-14-6.