Chromenes from the Brown Alga *Sargassum siliquastrum*

Kyoung Hwa Jang,[†] Bong Ho Lee,[‡] Byoung Wook Choi,[‡] Hyi-Seung Lee,[§] and Jongheon Shin*[,†]

Natural Products Research Institute, College of Pharmacy, Seoul National University, #28 Yungun, Jongro, Seoul 110-460, Korea, Department of Applied Chemistry, Hanbat National University, 16-1 Dukmyung, Yusung, Taejeon, 305-719, Korea, and Marine Natural Products Laboratory, Korea Ocean Research & Development Institute, Ansan P.O. Box 29, Seoul 425-600, Korea

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Sargachromanols A−P (**1**−**16**), sixteen new meroterpenoids of the chromene class, were isolated from the brown alga *Sargassum siliquastrum* collected from Jaeju Island, Korea. On the basis of the combined results of spectral and chemical analyses, the structures of the polyprenyl portions of these chromanol-containing compounds were determined to be linear triprenyls (**1** and **2**) and tetraprenyls (**3**−**11**), while others were the corresponding rearranged (**12**−**15**) and cyclized (**16**) tetraprenyls, respectively. The new compounds exhibited significant antioxidant activity in the DPPH assay. Compounds **7** and **15** also showed inhibitory activity toward butylcholine esterase.

Meroterpenoids of the chromene and related structural classes, consisting of a polyprenyl chain attached to a hydroquinone or similar aromatic rings, are widely distributed among marine organisms such as coelenterates, fish, macroalgae, sponges, and tunicates.[1] These metabolites, possessing diverse carbon skeletons and functionalities, are particularly abundant within brown algae (division Phaeophyta), which makes chromenes one of the representative groups of secondary metabolites of these organisms.[2] Brown algal-derived chromene metabolites exhibit cytotoxicity, antioxidant activity, and inducement of the larval settlement of a hydrozoan.[3−10] Chromenes from other marine organisms also possess diverse bioactive properties such as anticancer and antimutagenic activities as well as inhibitory activities against various enzymes.[11−17]

In the course of our continuing search for bioactive metabolites from marine organisms from Korea, we encountered the brown alga *Sargassum siliquastrum* (Mertens ex Turner, C. Agardh) (family Sargassaceae), whose crude organic extract displayed significant antioxidant activity (67% absorbance at 0.1 mg/mL in the DPPH assay). Herein we describe the structure elucidation and bioactivity of 16 new chromenes, sargachromanols A−P (**1**−**16**). Sargachromanols A and B possess a linear triprenyl carbon skeleton, while others possess the corresponding tetraprenyl skeletons. Structural features of particular uniqueness are modes of rearrangement and cyclization of sargachromanols L−P (**12**−**16**) that are unprecedented in metabolites of marine algae.

Results and Discussion

The brown alga *S. siliquastrum* was collected at the subtidal zone off the coast of Jaeju Island, Korea. The lyophilized specimens were repeatedly extracted with CH_2Cl_2, acetone, and MeOH, respectively. The crude extracts were combined and the solvents removed under vacuum. The crude extract was then fractionated employing solvent-partitioning. Guided by the combined results of bioassay and ^{1}H NMR analysis, separation of the moderately polar fractions was next accomplished by C_{18} reversed-phase vacuum flash chromatography, followed by reversed-phase and silica HPLC, to afford compounds **1**−**16**.

Sargachromanol A (**1**) was isolated as a colorless gum, which analyzed for $C_{22}H_{30}O_3$ by combined HREIMS and ^{13}C NMR spectrometry. The ^{13}C NMR data of this compound displayed 10 carbon signals in the aromatic/olefinic region (δ 155−110). This spectral feature, coupled with two distinct proton signals at δ 6.49 (1H, d, J = 2.8 Hz) and 6.40 (1H, d, J = 2.8 Hz) in the ^{1}H NMR spectra, revealed the presence of a hydroquinone-type moiety and three double bonds in the molecule. Also present in the NMR spectra were signals of an aldehyde at δ 9.38 (1H, s) and 195.3 (CH) in the ^{1}H and ^{13}C NMR data, respectively. A strong absorption band at 1685 cm^{-1} in the IR spectrum and absorption maximum at 225 nm in the UV spectrum suggested that the aldehyde was indeed an α,β-unsaturated one. Consideration of spectral data, in conjunction with the eight degrees of unsaturation inherent in the molecular formula, showed that sargachromanol A possessed an additional ring.

Given this information, the structure of compound **1** was determined by detailed interpretation of 2-D NMR data. Long-range correlations of the aromatic protons at δ 6.49 and 6.40 and upfield protons at δ 2.71 (2H, t, J = 6.8 Hz) and 2.14 (3H, s) with aromatic carbons in the g(gradient)-HMBC data readily established a 3-alkyl-5-methylhydroquinone moiety (Table 1). The ^{1}H COSY data showed direct spin couplings between the benzylic methylene protons at δ 2.71 and the methylene protons at δ 1.79 and 1.73. Long-range correlations of the carbon bearing these protons, at δ 31.4, and those at δ 75.2 and 39.5 with the methyl proton at δ 1.27 allowed a chromanol moiety to be constructed. Similarly, long-range correlations of the vinyl methyl protons at δ 1.74 and 1.63 with neighboring carbons, combined with the ^{1}H COSY correlations of the olefinic protons with upfield protons, defined the structure of the linear prenyl portion. The unsaturated aldehyde group was located at the terminal isopropyl part of the prenyl chain on the basis of long-range correlations between the aldehyde proton and neighboring carbons.

Compound **1** possessed double bonds at C-3′ and C-7′. Upfield shifts of the vinyl methyl carbons at δ 9.2 (C-10′) and 15.8 (C-11′), coupled with the NOESY cross-peaks H-6′/H-10′ and H-7′/H-9′, assigned the *E* geometry for these. The

* To whom correspondence should be addressed. Tel: 82 2 740 8919. Fax: 82 2 762 8322. E-mail: shinj@snu.ac.kr.
† Seoul National University.
‡ Hanbat National University.
§ Korea Ocean Research & Development Institute.

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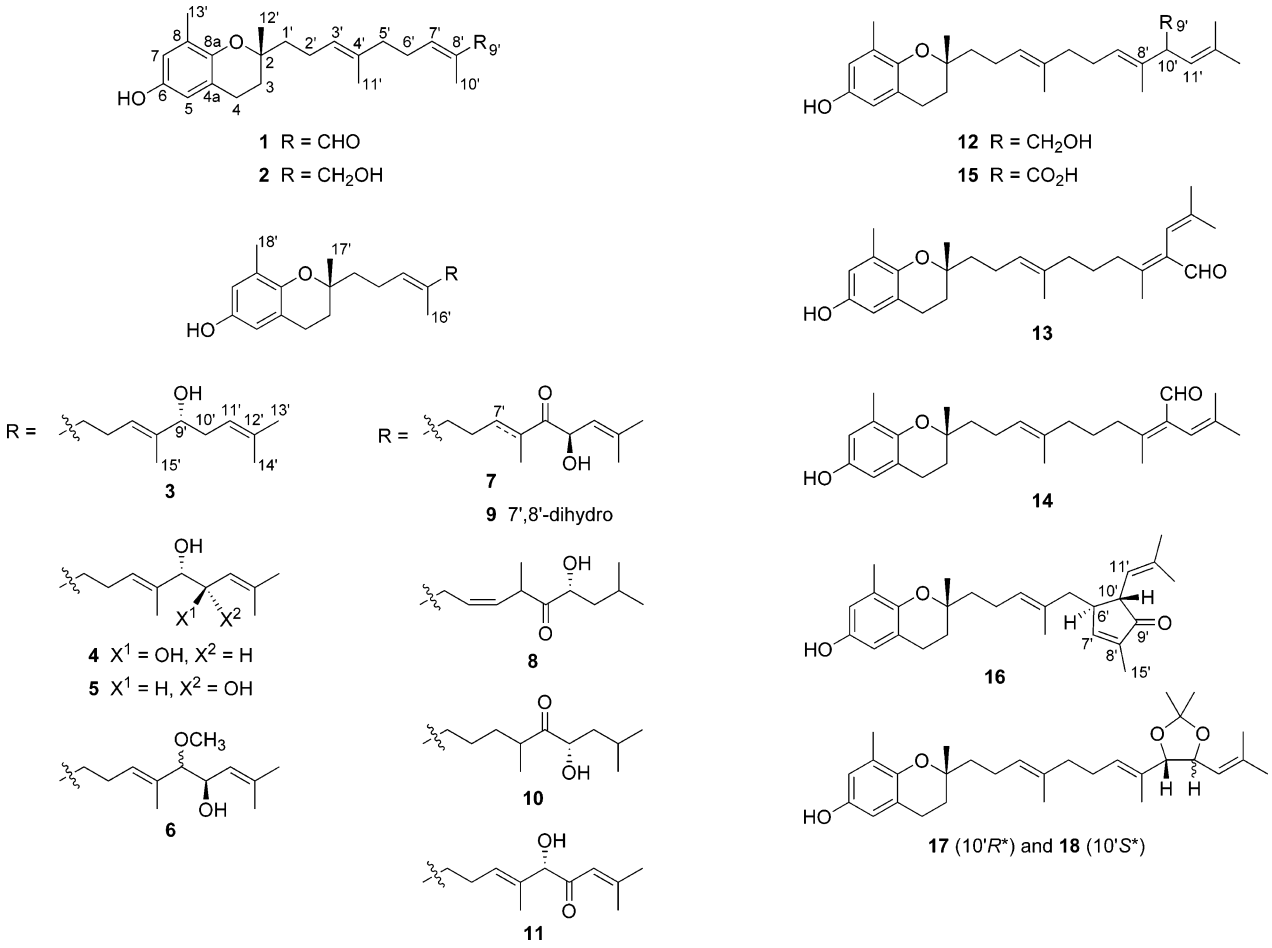
Chart 1



absolute stereochemistry at the C-2 asymmetric center was determined to be *R* on the basis of CD measurement (214 nm, +58.0; 248 nm, 0.0; 310 nm, −12.2) and application of Crabbe's rule.[18−20] Thus, the structure of sargachromanol A (**1**) was defined to be a chromene containing cyclized hydroquinone and triprenyl moieties.

The molecular formula of sargachromanol B (**2**) was deduced as $C_{22}H_{32}O_3$ by combined HREIMS and ^{13}C NMR analyses. The NMR spectra of this compound were highly compatible with those obtained for **1**, with the replacement of the aldehyde group with an oxymethylene (δ_H 3.98; δ_C 69.0) as the most noticeable difference. Also shifted con-

Table 1. ^1H and ^{13}C NMR Assignments for Compounds **1** and **2**[a]

	1		**2**	
position	δ_H	δ_C	δ_H	δ_C
2		75.2		75.3
3	1.79, dt (13.5, 6.8) 1.73, m	31.4	1.80, dt (13.7, 6.8) 1.73, dt (13.7, 6.8)	31.4
4	2.71, t (6.8)	22.5	2.70, t (6.8)	22.5
4a		121.2		121.2
5	6.40, d (2.8)	112.6	6.38, d (2.9)	112.6
6		147.8		147.7
7	6.49, d (2.8)	115.7	6.48, d (2.9)	115.6
8		127.4		127.4
8a		146.0		145.9
1′	1.63, m; 1.54, m	39.5	1.63, m; 1.54, m	39.6
2′	2.14, m	22.2	2.11, m	22.1
3′	5.19, tq (7.1, 1.0)	125.7	5.14, ddq (7.3, 6.8, 1.0)	124.6
4′		133.5		134.7
5′	2.16, t (7.3)	38.0	2.00, t (6.8)	39.2
6′	2.45, dt (7.3, 7.3)	27.4	2.12, m	26.2
7′	6.46, tq (7.3, 1.2)	154.4	5.38, ddq (7.3, 6.8, 1.0)	126.1
8′		139.4		134.7
9′	9.38, s	195.3	3.98, s	69.0
10′	1.74, br s	9.2	1.65, br s	13.7
11′	1.63, br s	15.8	1.59, br s	15.8
12′	1.27, s	24.0	1.26, s	24.0
13′	2.14, s	16.0	2.13, s	16.1

[a] NMR data were obtained in $CDCl_3$ solutions. Assignments were aided by a combination of ^1H COSY, TOCSY, gHSQC, and gHMBC experiments.

Table 2. ^{13}C NMR Assignments for the Tetraprenyl Portions of Compounds **3**−**15**

position	**3**[a]	**4**[a]	**5**[b]	**6**[a]	**7**[a]	**8**[a]	**9**[a]	**10**[a]	**11**[a]	**12**[a]	**13**[a]	**14**[a]	**15**[a]
2	75.3	75.2	76.2	75.2	75.0	75.2	75.2	75.3	75.2	75.3	75.2	75.3	75.3
3	31.4	31.3	32.8	31.4	31.4	31.4	31.3	31.4	31.4	31.4	31.4	31.4	31.4
4	22.5	22.4	23.4	22.5	22.4	22.4	22.4	22.5	22.4	22.5	22.5	22.5	22.5
1′	39.7	39.5	40.6	39.6	39.3	39.5	39.5	39.7	39.6	39.5	39.7	39.6	39.5
2′	22.2	22.1	23.2	22.1	22.1	22.2	22.1	22.1	22.1	22.1	22.1	22.2	22.1
3′	124.5	124.8	125.9	124.3	125.6	125.4	124.8	124.7	124.7	124.8	125.0	125.4	124.6
4′	134.8	134.6	135.8	134.9	133.5	133.0	134.3	134.6	134.5	134.8	134.4	134.1	134.7
5′	39.3	39.1	40.3	39.2	37.9	37.2	39.4	39.5	39.0	39.6	39.5	39.4	39.1
6′	26.2	26.0	27.2	26.3	27.4	130.6	25.3	25.5	26.6	26.2	25.2	27.9	26.5
7′	126.1	129.5	129.4	127.9	145.5	129.2	33.4	31.6	132.6	126.8	37.1	32.6	127.9
8′	136.7	133.5	135.6	133.4	133.6	40.5	41.2	41.4	132.7	134.5	160.0	160.6	132.1
9′	77.0	80.2	82.7	78.2	201.2	211.8	214.6	216.4	83.3	63.8	191.2	190.8	178.5
10′	34.2	69.2	71.4	79.2	69.7	73.0	74.2	73.6	199.3	50.2	138.0	135.3	53.2
11′	120.2	123.3	125.8	121.6	123.3	120.9	120.9	42.6	118.7	122.9	118.2	118.0	120.0
12′	134.6	139.2	136.9	139.1	138.0	140.7	140.0	24.9	159.8	135.0	149.4	137.9	135.5
13′	25.9	26.0	26.1	26.0	25.8	26.0	25.9	23.7	28.1	26.0	25.3	25.4	25.9
14′	18.0	18.6	18.5	18.5	18.2	18.5	18.6	21.2	21.3	18.2	19.8	19.8	18.0
15′	11.7	11.8	12.3	12.6	11.7	16.6	16.0	17.8	10.7	13.7	17.4	22.6	14.4
16′	15.9	15.7	15.9	15.9	15.7	16.3	15.6	15.7	15.8	15.7	15.6	15.7	15.8
17′	24.0	24.0	24.4	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.1	24.0
OCH_3				56.0									

[a,b] NMR data were obtained in $CDCl_3$ and CD_3OD solutions, respectively.

siderably in the NMR data are the chemical shifts of protons and carbons at the terminal isoprene unit. These spectral changes were accommodated by the replacement of the C-9′ aldehyde with a primary alcohol that was evidenced by combined 2-D NMR analyses as well as corresponding changes in the IR and UV data. The geometry at the C-7′ double bond was assigned as *E* on the basis of NOESY cross-peaks H-6′/H-10′ and H-7′/H-9′.

Sargachromanol C (**3**) was isolated as a colorless gum, which analyzed for $C_{27}H_{40}O_3$ by HRFABMS and ^{13}C NMR spectrometry. The chromanol nature of this compound was evident from the characteristic proton and carbon signals in the NMR data. A combination of 2-D NMR analyses, in particular, ^1H COSY and gHMBC experiments, defined the polyprenyl portion of the molecule to be a linear tetraprenyl chain. Interpretation of a proton spin system containing the oxymethine proton at δ 3.98 (dd, $J = 7.1$, 6.2 Hz), aided by long-range correlations between this methine (δ_C 77.0) and a neighboring vinyl methyl group (δ_H 1.62; δ_C 11.7), located a hydroxyl substituent at C-9′ of the prenyl chain (Tables 2 and 3). The absolute configuration of this newly appearing asymmetric center was assigned as *R* by application of Mosher's MTPA method. The *R* configuration of the chromanol moiety was corroborated by CD measurement (213 nm, + 22.2; 249 nm, 0; 294 nm, −0.3) and was identical to that of **1**.

The molecular formula of two isomeric metabolites, sargachromanols D (**4**) and E (**5**), which failed to display molecular ion clusters in mass analyses, was deduced as $C_{27}H_{40}O_4$ by HREIMS analyses of triacetylated analogues (molecular formula $C_{33}H_{46}O_7$). Comparison of the NMR data for these compounds with those of **3** revealed the identical chromanol nature of **4** and **5**. A combination of 2-D NMR experiments defined the structures of both compounds as tetraprenyl chromanols containing hydroxyl groups at C-9′ and C-10′. Significant differences between these compounds on the chemical shifts of protons and carbons at asymmetric centers and nearby positions (C-7′−C-12′, C-15′) in the NMR data as well as coupling constants of oxymethine protons (**4**, $J_{9',10'} = 6.6$ Hz, $J_{10',11'} = 8.8$ Hz; **5**, $J_{9',10'} = 7.8$ Hz, $J_{10',11'} = 9.3$ Hz) suggested that **4** and **5** were diastereomers of each other.

Stereochemical assignments of these compounds were accomplished by NOESY experiments on synthetic derivatives.[21] Treatment of **4** and **5** with 2,2-dimethoxypropane and PPTS in acetone yielded the corresponding cyclic ketals **17** and **18**, respectively. The structure determination of these derivatives as well as full assignments of proton signals was aided by 2-D NMR experiments. NOESY data of **17** positioned H-9′ and H-10′ within spatial proximity at *syn* orientation on the basis of cross-peaks H-9′/H-10′, H-9′/methyl (δ 1.40), H-10′/methyl (δ 1.40), H-10′/H-15′, and H-11′/H-15′ (Figure 1). Conversely, *anti* orientation for the same protons was assigned for **18** on the basis of its NOESY cross-peaks H-9′/methyl (δ 1.43), H-9′/H-11′, H-10′/methyl (δ 1.45), and H-10′/H-15′. Thus, the relative configurations of asymmetric centers were assigned as 9′*S**,10′*R** and 9′*S**,10′*S** for sargachromanols D (**4**) and E (**5**), respectively.

An analogous metabolite, sargachromanol F (**6**), was analyzed for $C_{28}H_{42}O_4$ by HRFABMS and ^{13}C NMR spectrometry. The spectral data of this compound were very similar to those of **4** and **5**, with the appearance of signals of a methoxy group (δ_H 3.26, δ_C 56.0) as the most significant change in the NMR spectra. Mutual long-range correlations with the C-9′ methine (δ_H 4.02, δ_C 78.2) in the gHMBC data located the methoxy group at this position. The absolute configuration at the C-10′ asymmetric center was assigned as *R* by MTPA analysis. The *S* configuration was suggested for the neighboring C-9′ on the basis of NOESY cross-peaks H-7′/H-9′, H-9′/H-11′, H-10′/H-14′, H-10′/H-15′, H-10′/OCH_3, H-11′/H-13′, H-11′/OCH_3, and H-14′/OCH_3, in conjunction with the coupling constant-based ($J_{9'10'} = 5.1$ Hz) Newman projection model study (Figure 2). Since it was unconfirmed by the measurement of $^2J_{C,H}$ between the C-9′and C-10′ and neighboring protons, however, the absolute configuration at C-9′ remained undetermined. Thus, the structure of sargachromanol F (**6**) was determined to be the 9′-methoxy derivative of sargachromanol D (**4**) or related compounds.

The molecular formula of sargachromanol G (**7**), $C_{27}H_{38}O_4$, was determined by HREIMS and ^{13}C NMR spectrometry. The ^{13}C NMR data for this compound were very similar to those of **4** and **5**, with the replacement of an oxymethine with a carbonyl carbon at δ 201.2 as the most significant difference. Corresponding changes were also observed in the ^1H NMR data in which the signal of an oxymethine proton disappeared (Tables 2 and 3). Combined analyses of 2-D NMR data located the carbonyl and remaining hydroxyl group at C-9′ and C-10′, respectively. Upon the

Table 3. ^{1}H NMR Assignments for Compounds **3**–**9**

position	**3**[a]	**4**[a]	**5**[b]	**6**[a]	**7**[a]	**8**[a]	**9**[a]
3	1.80, dt (13.5, 6.8) 1.74, m	1.78, m; 1.71, m	1.78, dt (13.2, 6.8) 1.72, dt (13.2, 6.8)	1.79, m 1.73, dt (13.5, 6.8)	1.78, dt, (13.2, 7.3) 1.72, dt (13.2, 6.8)	1.79, dt (13.2, 6.8) 1.73, dt (13.2, 6.8)	1.78, dt (13.7, 6.8) 1.73, dt (13.7, 6.8)
4	2.71, t (6.8)	2.68, t (6.8)	2.67, t (6.8)	2.69, t (6.8)	2.71, ddd (16.6, 2.69, t (6.8) 7.3, 6.8); 2.65, ddd 16.6, 7.3, 6.8)	2.69, m	
5	6.39, d (2.5)	6.37, d (2.7)	6.31, d (2.4)	6.38, d (2.7)	6.38, d (2.7)	6.38, d (2.7)	6.38, d (2.9)
7	6.49, d (2.5)	6.46, d (2.7)	6.40, d (2.4)	6.47, d (2.7)	6.47, d (2.7)	6.48, d (2.7)	6.48, d (2.9)
1′	1.63, m; 1.55, m	1.62, dt (15.1, 7.3) 1.53, m	1.60, m; 1.52, m	1.62, m; 1.56, m	1.62, m; 1.52, m	1.62, m; 1.53, m	1.62, m; 1.53, m
2′	2.13, m	2.11, dt (7.3, 7.3)	2.13, dt (6.8, 7.3)	2.10, m	2.12, m	2.14, dt (7.3, 7.3)	2.10, m
3′	5.15, t (7.1)	5.13, t (7.3)	5.15 (6.8)	5.14, tq (7.1, 1.2)	5.13, t (7.3)	5.15, tq (7.3, 1.0)	5.11, t (7.3)
5′	2.01, dd (7.9, 7.1)	2.02, t (7.8)	1.97, t (7.3)	1.98, dd (8.4, 6.6)	2.08, t (7.3)	2.73, dd (15.6, 8.3) 2.67, dd (15.6, 6.8)	1.93, dd (6.8, 5.4)
6′	2.11, m	2.16, m	2.08, dt (6.8, 7.3)	2.12, m	2.34, dt (7.3, 7.3)	5.53, ddd (10.7, 8.3, 6.8)	1.32, m
7′	5.38, t (6.8)	5.46, t (7.3)	5.34, t (6.8)	5.41, tq (6.8, 1.2)	6.55, t (7.3)	5.30, dd (10.7, 10.7)	1.32, m
8′						3.67, dq (10.7, 6.8)	2.69, m
9′	3.98, dd (7.1, 6.2)	3.86, d (6.6)	3.71, d (7.8)	4.02, br d (5.1)			
10′	2.29, ddd (14.4, 7.1, 6.8); 2.20 m	4.30, dd (8.8, 6.6)	4.22, dd (9.3, 7.8)	3.95, dd (9.1, 5.1)	5.29, d (9.8)	4.88, d (10.3)	4.87, d (9.8)
11′	5.10, t (6.8)	5.19, dq (8.8, 1.5)	5.03, br d (9.3)	5.09, dh (9.1, 1.2)	4.99, dh (9.8, 1.5)	4.98, dh (10.3, 1.5)	4.98, br d (9.8)
13′	1.73, s	1.77, s	1.67, d (1.0)	1.78, d (1.2)	1.72, s	1.80, d (1.5)	1.80, s
14′	1.64, s	1.73, s	1.66, d (1.5)	1.69, d (1.2)	1.82, s	1.81, d (1.5)	1.85, d (1.5)
15′	1.62, s	1.65, s	1.55, s	1.61, d (1.2)	1.80, s	1.13, d (6.8)	1.05, d (6.4)
16′	1.61, s	1.59, s	1.57, s	1.59, s	1.59, s	1.59, s	1.56, s
17′	1.27, s	1.25, s	1.24, s	1.26, s	1.25, s	1.25, s	1.26, s
18′	2.12, s	2.12, s	2.07, s	2.12, s	2.11, s	2.12, s	2.12, s
OCH_3				3.26, s			

[a,b] NMR data were obtained in $CDCl_3$ and CD_3OD solutions, respectively.

result of MTPA analysis, the 10′*R* configuration was assigned for this compound.

A closely related metabolite, sargachromanol H (**8**), was analyzed for $C_{27}H_{38}O_4$ by HREIMS and ^{13}C NMR analyses. The NMR data for this compound were highly compatible with those from compound **7**. However, the DEPT experiment revealed the replacement of a trisubstituted double bond of **7** with a disubstituted one in **8**. Corresponding differences were also found in the ^{1}H NMR data, in which newly appearing signals were observed at δ 5.53, 5.30, and 1.13 (Table 2). A combination of ^{1}H COSY, TOCSY, and gHMBC experiments showed the shift of the C-7′ double bond of **7** to C-6′ in **8**. This newly formed double bond was assigned a *Z* geometry on the basis of the coupling constant ($J_{6',7'}$ = 10.7 Hz) between the olefinic protons. The 10′*R* configuration, identical to **7**, was assigned for this compound by MTPA analysis.

The molecular formulas of two closely related metabolites, sargachromanols I (**9**) and J (**10**), were deduced as $C_{27}H_{40}O_4$ and $C_{27}H_{42}O_4$, respectively, by HREIMS and ^{13}C NMR analyses. The NMR data for these compounds were very similar to those of compound **7**. A combination of 2-D NMR experiments readily defined the structures of **9** and **10** as the 7′,8′-dihydro and 7′,8′,11′,12′-tetrahydro derivatives of **7**, respectively. On the basis of the results of MTPA analysis, the 10′*R* configuration, identical to **7**, was assigned for **9**, while the opposite 10′*S* configuration was assigned for **10**, respectively.

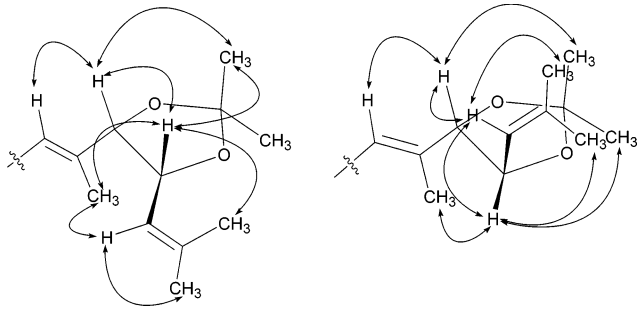


Figure 1. Selected NOE correlations for the ketals **17** (left) and **18** (right).

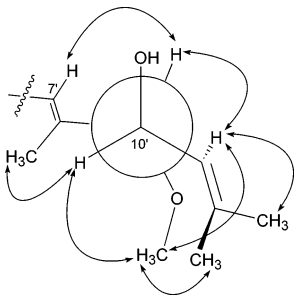


Figure 2. Solution conformation of C-9′ and C-10′ asymmetric centers and neighboring positions of 6 on the basis of NOESY interpretation.

Table 4. ^{1}H NMR Assignments for Compounds **10**−**15**[a]

position	10	11	12	13	14	15
3	1.80, dt (13.6, 7.2) 1.73, dt (13.6, 6.7)	1.79, dt (13.7, 6.8) 1.73, dt (13.7, 6.8)	1.79, dt (13.2, 7.1) 1.74, m	1.79, dt (13.8, 6.9) 1.73, dt (13.8, 6.9)	1.79, dt (13.5, 6.8) 1.74, dt (13.5, 6.8)	1.79, dt (13.5, 6.6) 1.74, m
4	2.69, m	2.69, t (6.8)	2.69, t (7.1)	2.70, t (6.9)	2.70, t (6.8)	2.69, t (6.6)
5	6.38, d (2.7)	6.38, d (2.9)	6.38, d (2.7)	6.38, d (2.9)	6.38, d (2.7)	6.38, d (2.7)
7	6.47, d (2.7)	6.47, d (2.9)	6.47, d (2.7)	6.48, d (2.9)	6.48, d (2.7)	6.48, d (2.7)
1′	1.64, m; 1.54, m	1.64, dt (15.1, 7.1) 1.54, dt (15.1, 8.3)	1.62, m; 1.54, m	1.63, m; 1.54, m	1.63, m; 1.54, m	1.63, m; 1.54, m
2′	2.10, dt (6.8, 7.3)	2.13, m	2.11, m	2.12, m	2.12, m	2.10, m
3′	5.12, br t (6.8)	5.17, t (6.8)	5.12, t (6.8)	5.13, tq (6.9, 1.2)	5.15, t (6.8)	5.12, t (6.8)
5′	1.94, t (7.3)	2.05, t (7.3)	2.01, t (7.1)	1.95, t (7.3)	2.02, t (7.4)	2.00, t (7.2)
6′	1.30, m	2.18, m	2.12, m	1.54, m	1.64, m	2.12, m
7′	1.28, m	5.61, t (6.8)	5.21, t (6.8)	2.14, m	2.55, dd (8.1, 7.7)	5.33, t (6.8)
8′	2.70, m					
9′		4.43, s	3.50, dd (10.1, 8.4) 3.40, dd (10.1, 6.6)	10.06, s	10.03, s	
10′	4.29, br d (10.5)		3.05, ddd (9.2, 8.4, 6.6)			3.85, d (9.3)
11′	1.47, m; 1.30, m	6.13, br s	5.03, br d (9.2)	5.59, br s	5.64, br s	5.39, dh (9.3, 1.2)
12′	1.97, m					
13′	0.97, d (6.7)	1.92, s	1.72, s	1.82, d (1.2)	1.84, d (1.0)	1.75, d (1.2)
14′	1.00, d (6.6)	2.22, s	1.64, d (0.8)	1.45, d (1.2)	1.45, br s	1.62, d (1.2)
15′	1.10, d (7.1)	1.42, s	1.56, s	2.20, d (1.2)	1.87, s	1.65, s
16′	1.56, s	1.61, s	1.58, s	1.57, br s	1.58, br s	1.58, s
17′	1.25, s	1.26, s	1.26, s	1.26, s	1.26, s	1.26, s
18′	2.12, s	2.12, s	2.13, s	2.12, s	2.13, s	2.12, s
OH	3.39, d (5.1)					

[a] NMR data were obtained in $CDCl_3$ solutions.

The molecular formula of sargachromanol K (**11**) was deduced as $C_{27}H_{38}O_4$ by HREIMS and ^{13}C NMR spectrometry. The NMR data for this compound were reminiscent of those from compound **7**, suggesting the presence of identical functionalities in **11**. However, detailed examination of the ^{1}H and ^{13}C NMR data revealed significant shifts of carbons and protons at the terminus (C-7′−C-15′) of the prenyl chain (Tables 3 and 4). Combined 2-D NMR analyses located the carbonyl and hydroxyl groups at C-10′ and C-9′, respectively, opposite from **7** and other sargachromanols. The 9′*S* configuration was assigned for the newly appearing asymmetric center by MTPA analysis.

Sargachromanol L (**12**) was isolated as a colorless gum, which analyzed for $C_{27}H_{40}O_3$ by HREIMS and ^{13}C NMR spectrometry. The NMR spectra of this compound displayed the characteristic proton and carbon signals of a chromanol. However, the ^{13}C NMR and DEPT data revealed the presence of seven methyl-equivalent groups (six methyl groups and one primary alcohol) instead of six methyl-equivalents of other tetraprenyl chromanols. A combination of 2-D NMR experiments indicated the variation of the carbon framework at the terminal isoprene unit. That is, the ^{1}H COSY experiment defined a spin system that consisted of the oxymethylene protons at δ 3.50 and 3.40, a methine proton at δ 3.05, and an olefinic proton at δ 5.03 in a linear array that was consistent with the gHMBC correlations between these protons and carbons bearing them (Tables 3 and 4). Additional long-range correlations were also found between the methine carbon at δ 50.2 and the vinyl methyl proton H-15′ as well as between the olefinic carbons at δ 135.0 and 122.9 and terminal methyl protons H-13′ and H-14′. The NMR data were accommodated by a rearrangement of the prenyl portion of compound **12** in which the C-8′−C-9′ bond of a linear tetraprenyl moiety migrated to C-8′−C-10′. Thus, the structure of sargachromenal L (**12**) was defined as a tetraprenyl chromanol possessing a rearranged carbon skeleton.

The molecular formulas of two isomeric compounds, sargachromanols M (**13**) and N (**14**), were assigned as $C_{27}H_{38}O_3$ by high-resolution mass and ^{13}C NMR spectrometry. The NMR data of these compounds were very similar to those of compound **12**, with the replacement of the oxymethylene group of **12** with an aldehyde (**13**, δ_H 10.06, δ_C 191.2; **14**, δ_H 10.03, δ_C 190.8) as the most significant change (Tables 3 and 4). In addition, the IR absorption bands (**13**, 1665 cm^{-1}; **14**, 1660 cm^{-1}) and UV absorption maxima (225 nm for both) suggested the presence of an α,β-unsaturated aldehyde group in these compounds. A combination of NMR analyses, in particular, long-range correlations between the aldehyde and vinyl methyl protons with neighboring carbons in the gHMBC data, located the aldehyde group at C-9′ of the rearranged skeleton as well as the migration of a double bond of **12** from C-7′ to C-8′(C-10′) in **13** and **14**.

Comparison of the NMR data between **13** and **14** revealed noticeable shifts of protons and carbons at the terminal two isoprene units (C-6′−C-15′). A NOESY experiment of **13** showed cross-peaks H-7′/H-11′ and H-10′/H-15′ assigning the *E* configuration at the C-8′ double bond. Contrarily, the same experiment determined the opposite *Z* configuration for **14** on the basis of cross-peaks H-7′/H-10′, H-10′/H-14′, and H-11′/H-15′. Thus, sargachromanols M and N were defined as aldehyde-bearing chromanols isomeric to each other.

The molecular formula of an analogous compound, sargachromanol O (**15**), was established as $C_{27}H_{38}O_4$ by high-resolution mass and ^{13}C NMR analyses. The spectral data for this compound were very similar to those of compound **12**. The replacement of the C-10′ oxymethylene with a carboxyl group at δ 178.5 in the ^{13}C NMR data was deduced by detailed 2-D NMR analyses and IR measurement (1705 cm^{-1}).

Last, sargachromanol P (**16**) was isolated as a colorless gum, and its molecular formula was assigned as $C_{27}H_{36}O_3$ by combined HRFABMS and ^{13}C NMR spectrometry. The NMR data for this compound showed the characteristic proton and carbon signals of a chromanol. However, preliminary examination of the ^{13}C NMR and DEPT data revealed significant differences in carbon signals from the terminal two isoprene units, which, in conjunction with 10

Table 5. ^{1}H and ^{13}C NMR Assignments for Compound **1**[a]

position	δ_H	δ_C		gHMBC
2		75.2	C	
3	1.78, dt (14.0, 6.8)	31.4	CH_2	C-2, C-4, C-4a, C-1′, C-17′
	1.72, m			
4	2.69, m	22.4	CH_2	C-2, C-3, C-4a, C-5, C-8a
4a		121.1	C	
5	6.38, d (2.7)	112.6	CH	C-4, C-6, C-7, C-8a
6		147.9	C	
7	6.48, d (2.7)	115.7	CH	C-5, C-6, C-8a, C-18′
8		127.3	C	
8a		145.9	C	
1′	1.64, m; 1.53, m	39.5	CH_2	C-2, C-3, C-2′, C-3, C-17′
2′	2.13, m	22.2	CH_2	C-2, C-1′
3′	5.20, t (7.1)	126.9	CH	C-1′, C-2′, C-5′, C-16′
4′		132.7	C	
5′	2.16, dd (14.7, 8.1)	44.5	CH_2	C-3′, C-4′, C-6′, C-7′, C-10′, C-16′
	2.09, dd (14.7, 5.4)			
6′	2.65, m	45.5	CH	C-7′
7′	7.18, br d (1.1)	160.4	CH	C-5′, C-6′, C-8′, C-9′, C-10′, C-15′
8′		140.2	C	
9′		210.2	C	
10′	2.83, dd (9.5, 2.3)	52.3	CH	C-5′, C-6′, C-7′, C-9′, C-11′, C-12′
11′	4.88, br d (9.5)	121.4	CH	C-6′, C-10′, C-13′, C-14′
12′		136.1	C	
13′	1.66, d (1.1)	18.4	CH_3	C-11′, C-12′, C-14′
14′	1.72, br s	25.8	CH_3	C-11′, C-12′, C-13′
15′	1.75, dd (1.6, 1.6)	10.4	CH_3	C-7′, C-8′, C-9′
16′	1.60, s	15.9	CH_3	C-3′, C-4′, C-5′
17′	1.26, s	24.0	CH_3	C-2, C-3, C-1′
18′	2.13, s	16.0	CH_3	C-7, C-8, C-8a

[a] NMR data were obtained in $CDCl_3$ solutions. Assignments were aided by ^{1}H COSY, TOCSY, gHSQC, and gHMBC experiments.

degrees of unsaturation inherent in the molecular formula, suggested the presence of an additional ring at the prenyl portion. The structural difference was thought to be associated with the carbon signals of a carbonyl and trisubstituted double bond at δ 210.2 (C), 160.4 (CH), and 140.2 (C), respectively, in the ^{13}C NMR data (Table 5). A corresponding proton signal at δ 7.18 (1H, br d, J = 1.1 Hz) in the ^{1}H NMR data as well as the IR absorption band (1690 cm^{-1}) and UV absorption maximum (224 nm) showed that the newly created carbons formed a cyclic α,β-unsaturated ketone.

A combination of 2-D NMR data revealed that the chromanol moiety and nearby portion (C-2−C-5′) of other sargachromanols are intact in compound **16**. Beginning with the methylene signals at δ 2.16 and 2.09 in the ^{1}H NMR spectra, a proton spin system was traced to include methine protons at δ 2.65, 2.83, and 4.88 in a linear array by the ^{1}H COSY and TOCSY experiments. Also found by these experiments was small (J = 1.1 Hz) but consistent coupling between the methine proton at δ 2.65 and olefinic proton at δ 7.18. Long-range couplings of this olefinic proton with carbons at δ 52.3 (CH), 45.5 (CH), and 44.5 (CH_2) bearing protons at δ 2.83, 2.65, 2.16, and 2.09, and the carbonyl and olefinic carbons at δ 210.2 and 140.2, respectively, allowed a cyclopentenone moiety to be constructed (Table 5). Attachment of a vinyl methyl group at C-2 of this moiety (C-15′ of the molecule) was secured by long-range couplings of the methyl proton at δ 1.75 with the carbonyl and olefinic carbons. Similarly, an isobutylene group was placed at C-5 of the cyclopentenone ring (C-10′ of the molecule) on the basis of long-range correlations between the protons and carbons of the isobutylene and neighboring positions.

The cyclopentenone moiety possessed two asymmetric centers at C-6′ and C-10′. NOESY cross-peaks H-5′/H-10′, H-5′/H-7′, and H-6′/H-11′ assigned *anti* orientation for H-5′ and H-10′ on the cyclopentenone ring, thus 5′*R**,10′*S** configurations for the asymmetric centers. Thus, the structure of sargachromanol P (**16**) was determined to be a chromanol containing a cyclized tetraprenyl moiety. Meroterpenoids derived from brown algae possess diverse carbon skeletons at their polyprenyl portion.[1,2] To the best of our knowledge, however, the cyclization pattern of sargachromanol P is unprecedented in marine algae.

Chromenes and related hydroquinone-derived compounds such as tocotrienols are recognized to exhibit antioxidant activity.[3,14,17] In our measurement using DPPA (1,1-diphenyl-2-picrylhydrazyl), all of the sargachromanols A−P (**1**−**16**) exhibited significant radical scavenging activity in the range of 87−91% at the concentration of 100 μg/mL: **1**, 87.4; **2**, 90.0; **3**, 90.5; **4**, 89.6; **5**, 87.3; **6**, 88.2; **7**, 90.4; **8**, 87.8; **9**, 90.4; **10**, 89.1; **11**, 89.2; **12**, 90.1; **13**, 88.7; **14**, 89.2; **15**, 88.7; **16**, 88.8%. In addition, compounds **7** and **15** displayed 82.7 and 80.0%, respectively, inhibition toward butylcholine esterase at the same concentration, while other sargachromanols showed weaker or negligible activity.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a JASCO P-102 digital polarimeter using a 5 cm cell. CD data were obtained on a JASCO J-715 spectropolarimeter in MeOH solutions. IR spectra were recorded on a JASCO FT/IR-5300 spectrophotometer. UV spectra were recorded on a Hitachi U-3210 spectrophotometer. NMR spectra were recorded in $CDCl_3$ and CD_3OD solutions containing Me_4Si as internal standard, on Bruker AMX-500 and Varian Gemini-2000 spectrometers. Proton and carbon NMR spectra were measured at 500 (300 MHz for Gemini-2000) and 125 MHz, respectively. Mass spectra were obtained on JEOL JMS-SX 102A and JMS-700 high-resolution mass spectrometers for EI and FAB experiments, respectively, and provided by the Korea Basic Science Institute Seoul Branch, Seoul, Korea. All solvents used were spectral grade or were distilled from glass prior to use.

Plant Material. *Sargassum siliquastrum* (sample number M301) was collected by hand at the subtidal zone (0−2 m) off the southwestern shore of Jaeju Island, Korea, in April 2003. A voucher specimen is currently on deposit in the Algal Collection, Hanbat National University, Taejeon, Korea, under the curatorship of B.W.C.

Extraction and Isolation. The fresh collection was immediately frozen and kept at −25 °C until chemically investigated. The specimens were lyophilized (dry wt 350 g), macerated, and repeatedly extracted with CH_2Cl_2 (4 L × 2), acetone (4 L × 2), and MeOH (4 L × 1). The combined crude extract (41.6 g) was partitioned between 15% aqueous MeOH (36.2 g) and *n*-hexane (4.9 g). An aliquot (25.2 g) of the aqueous MeOH layer was separated by C_{18} reversed-phase vacuum flash chromatography using sequential mixtures of MeOH and H_2O as eluents (elution order: 50%, 40%, 30%, 20%, 10% aqueous MeOH, 100% MeOH) and finally acetone. On the basis of the results of TLC analysis, the fractions eluted with 30−20% aqueous MeOH were combined (710 mg) and separated by C_{18} reversed-phase HPLC (YMC ODS-A column, 25% aqueous MeOH) to yield, in order of elution, compounds **2**, **4**, **1**, **8**, **7**, **5**, **11**, and **9** as colorless gums. Purifications of these metabolites were then accomplished by silica HPLC (YMC-silica column, 35% EtOAc in *n*-hexane for **2** and **5**, 30% EtOAc in *n*-hexane for others). The purified metabolites were isolated in the following amounts: 4.9, 5.1, 57.2, 52.3, 217.9, 10.1, 127.4, and 16.3 mg of **1**, **2**, **4**, **5**, **7**−**9**, and **11**, respectively.

The fraction (870 mg) eluted with 10% aqueous MeOH was separated by reversed-phase HPLC (20% aqueous MeOH) to yield, in order of elution, compounds **16**, **6**, **10**, **15**, **13**, **14**, **12**, and **3** as colorless gums. Final purification was then accomplished by silica HPLC (YMC-silica column, 30% EtOAc in *n*-hexane) to afford 4.9, 10.3, 20.6, 6.1, 8.0, 5.2, 10.9, and 10.1 mg of **3**, **6**, **10**, and **12**−**16**, respectively.

Sargachromanol A (1): colorless gum; $[\alpha]^{20}_D$ +15.8° (*c* 0.12, MeOH); IR (NaCl) ν_{max} 3400−3300, 2925, 1685, 1470, 1220 cm^{-1}; UV (MeOH) λ_{max} (log ϵ) 225 (3.84) nm; ^{1}H and ^{13}C NMR data, see Table 1; HREIMS *m/z* 342.2192 [M]$^+$ (calcd for $C_{22}H_{30}O_3$, 342.2195).

Sargachromanol B (2): colorless gum; $[\alpha]^{20}_D$ +14.6° (*c* 0.10, MeOH); IR (NaCl) ν_{max} 3400−3300, 2975, 2930, 1470, 1225 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 1; HREIMS *m/z* 344.2356 [M]$^+$ (calcd for $C_{22}H_{32}O_3$, 344.2351).

Sargachromanol C (3): colorless gum; $[\alpha]^{20}_D$ +10.6° (*c* 0.09, MeOH); IR (NaCl) ν_{max} 3400−3300, 2930, 1645, 1475, 1220 cm^{-1}; ^{1}H and ^{13}C NMR, see Tables 3 and 2, respectively; HRFABMS *m/z* 435.2880 [M + Na]$^+$ (calcd for $C_{27}H_{40}O_3Na$, 435.2875).

Sargachromanol D (4): colorless gum; $[\alpha]^{20}_D$ +19.4° (*c* 0.16, MeOH); IR (NaCl) ν_{max} 3400−3300, 2975, 2930, 1470, 1375, 1220 cm^{-1}; ^{1}H and ^{13}C NMR, see Tables 3 and 2, respectively; HREIMS (triacetate) *m/z* 554.3244 [M]$^+$ (calcd for $C_{33}H_{46}O_7$, 554.3244).

Sargachromanol E (5): colorless gum; $[\alpha]^{20}_D$ +14.4° (*c* 0.12, MeOH); IR (NaCl) ν_{max} 3400−3300, 2975, 2930, 1645, 1470 cm^{-1}; ^{1}H and ^{13}C NMR, see Tables 3 and 2, respectively; HREIMS (triacetate) *m/z* 554.3239 [M]$^+$ (calcd for $C_{33}H_{46}O_7$, 554.3244).

Sargachromanol F (6): colorless gum; $[\alpha]^{20}_D$ +27.0° (*c* 0.14, MeOH); IR (NaCl) ν_{max} 3400−3300, 2930, 1470, 1220 cm^{-1}; ^{1}H and ^{13}C NMR, see Tables 3 and 2, respectively; HRFABMS *m/z* 465.2994 [M + Na]$^+$ (calcd for $C_{28}H_{42}O_4Na$, 465.2981).

Sargachromanol G (7): colorless gum; $[\alpha]^{20}_D$ −79.2° (*c* 0.12, MeOH); IR (NaCl) ν_{max} 3400−3300, 2970, 2930, 1665, 1470, 1220 cm^{-1}; UV (MeOH) λ_{max} (log ϵ) 230 (3.80) nm; ^{1}H and ^{13}C NMR, see Tables 3 and 2, respectively; HREIMS *m/z* 426.2774 [M]$^+$ (calcd for $C_{27}H_{38}O_4$, 426.2770).

Sargachromanol H (8): colorless gum; $[\alpha]^{20}_D$ −143.0° (*c* 0.10, MeOH); IR (NaCl) ν_{max} 3400−3300, 2975, 2930, 1715, 1470, 1460, 1220 cm^{-1}; ^{1}H and ^{13}C NMR, see Tables 3 and 2, respectively; HREIMS *m/z* 426.2769 [M]$^+$ (calcd for $C_{27}H_{38}O_4$, 426.2770).

Sargachromanol I (9): colorless gum; $[\alpha]^{20}_D$ −118.2° (*c* 0.11, MeOH); IR (NaCl) ν_{max} 3400−3300, 2935, 1710, 1470, 1220 cm^{-1}; ^{1}H and ^{13}C NMR, see Tables 3 and 2, respectively; HREIMS *m/z* 428.2924 [M]$^+$ (calcd for $C_{27}H_{40}O_4$, 428.2927).

Sargachromanol J (10): colorless gum; $[\alpha]^{20}_D$ +8.2° (*c* 0.14, MeOH); IR (NaCl) ν_{max} 3400−3300, 2935, 1700, 1470, 1220 cm^{-1}; ^{1}H and ^{13}C NMR, see Tables 4 and 2, respectively; HREIMS *m/z* 430.3076 [M]$^+$ (calcd for $C_{27}H_{42}O_4$, 430.3083).

Sargachromanol K (11): colorless gum; $[\alpha]^{20}_D$ +175.6° (*c* 0.11, MeOH); IR (NaCl) ν_{max} 3400−3300, 2930, 1680, 1620, 1470, 1220 cm^{-1}; UV (MeOH) λ_{max} (log ϵ) 237 (3.77) nm; ^{1}H and ^{13}C NMR, see Tables 4 and 2, respectively; HREIMS *m/z* 426.2768 [M]$^+$ (calcd for $C_{27}H_{38}O_4$, 426.2770).

Sargachromanol L (12): colorless gum; $[\alpha]^{20}_D$ +17.6° (*c* 0.13, MeOH); IR (NaCl) ν_{max} 3400−3300, 2925, 1475, 1375, 1220 cm^{-1}; ^{1}H and ^{13}C NMR, see Tables 4 and 2, respectively; HREIMS *m/z* 412.2979 [M]$^+$ (calcd for $C_{27}H_{40}O_3$, 412.2977).

Sargachromanol M (13): colorless gum; $[\alpha]^{20}_D$ +11.8° (*c* 0.12, MeOH); IR (NaCl) ν_{max} 3400−3300, 2930, 1665, 1655, 1475, 1465, 1220 cm^{-1}; UV (MeOH) λ_{max} (log ϵ) 225 (3.97) nm; ^{1}H and ^{13}C NMR, see Tables 4 and 2, respectively; HREIMS *m/z* 410.2820 [M]$^+$ (calcd for $C_{27}H_{38}O_3$, 410.2821).

Sargachromanol N (14): colorless gum; $[\alpha]^{20}_D$ +10.0° (*c* 0.12, MeOH); IR (NaCl) ν_{max} 3400−3300, 2930, 1660, 1655, 1470, 1220 cm^{-1}; UV (MeOH) λ_{max} (log ϵ) 225 (3.95) nm; ^{1}H and ^{13}C NMR, see Tables 4 and 2, respectively; HREIMS *m/z* 410.2818 [M]$^+$ (calcd for $C_{27}H_{38}O_3$, 410.2821).

Sargachromanol O (15): colorless gum; $[\alpha]^{20}_D$ +12.9° (*c* 0.11, MeOH); IR (NaCl) ν_{max} 3400−3300, 2930, 1705, 1470, 1220 cm^{-1}; ^{1}H and ^{13}C NMR, see Tables 4 and 2, respectively; HREIMS *m/z* 426.2769 [M]$^+$ (calcd for $C_{27}H_{38}O_4$, 426.2770).

Sargachromanol P (16): colorless gum; $[\alpha]^{20}_D$ +14.7° (*c* 0.16, MeOH); IR (NaCl) ν_{max} 3400−3300, 2925, 1690, 1635, 1220 cm^{-1}; UV (MeOH) λ_{max} (log ϵ) 224 (3.86) nm; ^{1}H NMR and ^{13}C NMR data, see Table 5; HRFABMS *m/z* 431.2574 [M + Na]$^+$ (calcd for $C_{27}H_{36}O_3Na$, 431.2562).

MTPA Esterification of Sargachromanol C (3). Prepared as described previously.[22] From 1.5 and 1.8 mg of compound **3** were obtained 1.5 and 1.6 mg of (*S*)- and (*R*)-MTPA ester, **3S** and **3R**, respectively. **3S**: ^{1}H NMR ($CDCl_3$) δ 7.65 (phenyl), 7.50−7.33 (phenyl), 6.708 (H-7), 6.679 (H-5), 5.456 (H-7′), 5.316 (H-9′), 5.123 (H-3′), 5.033 (H-11′), 3.677 (OCH_3), 3.538 (OCH_3), 2.749 (H-4), 2.473 (H-10′), 2.263 (H-10′), 2.156 (H-18′), 2.104 (H-6′), 1.995 (H-5′), 1.684 (H-13′), 1.591 (H-14′), 1.590 (H-16′), 1.468 (H-15′), 1.277 (H-17′). **3R**: ^{1}H NMR ($CDCl_3$) δ 7.64 (phenyl), 7.50−7.33 (phenyl), 6.709 (H-7), 6.679 (H-5), 5.532 (H-7′), 5.369 (H-9′), 5.128 (H-3′), 4.920 (H-11′), 3.678 (OCH_3), 3.513 (OCH_3), 2.746 (H-4), 2.417 (H-10′), 2.230 (H-10′), 2.157 (H-18′), 2.129 (H-6′), 1.995 (H-5′), 1.622 (H-13′, H-15′), 1.594 (H-16′), 1.533 (H-14′), 1.270 (H-17′). $\Delta\delta$(**3S**−**3R**): H-4, +0.003 ppm; H-5, 0 ppm; H-7, −0.001 ppm; H-3′, −0.005 ppm; H-5′, 0 ppm; H-6′, −0.025 ppm; H-7′, −0.076 ppm; H-9′, −0.053 ppm; H-10′, +0.056, +0.033 ppm; H-11′, +0.113 ppm; H-13′, +0.062 ppm; H-14′, +0.058 ppm; H-15′, −0.154 ppm; H-16′, −0.004 ppm; H-17′, +0.007 ppm; H-18′, −0.001 ppm.

Ketal Formation of Sargachromanol D (4). To a stirred solution of 3.1 mg of **4** in 3 mL of dry pyridine were added 0.2 mL of 2,2-dimethoxypropane and 1.5 mg of PPTS. The mixture was refluxed under N_2 for 30 min. To quench the reaction, 0.2 mL of Et_3N was added and the resulting mixture refluxed for 15 min. The mixture was filtered by using a silica Sep-pak column (25% EtOAc in *n*-hexane). The cyclic ketal (**17**) was purified by silica HPLC (15% EtOAc in *n*-hexane), 2.2 mg: ^{1}H NMR ($CDCl_3$) δ 6.48 (1H, d, J = 2.8 Hz, H-7), 6.39 (1H, d, J = 2.8 Hz, H-5), 5.44 (1H, t, J = 7.1 Hz, H-7′), 5.15 (1H, t, J = 7.0 Hz, H-3′), 5.12 (1H, d, J = 8.8 Hz, H-11′), 4.94 (1H, dd, J = 8.8, 7.1 Hz, H-10′), 4.52 (1H, d, J = 7.1 Hz, H-9′), 2.70 (2H, m, H-4), 2.13 (3H, s, H-18′), 2.12 (2H, m, H-6′), 2.10 (2H, m, H-2′), 2.00 (2H, t, J = 7.8 Hz, H-5′), 1.78 (1H, dt, J = 13.2, 6.8 Hz, H-3), 1.74 (1H, dt, J = 13.2, 6.8 Hz, H-3), 1.71 (3H, s, H-13′), 1.67 (3H, s, H-14′), 1.61 (1H, m, H-1′), 1.60 (3H, s, H-16′), 1.55 (1H, m, H-1′), 1.53 (3H, s, ketal), 1.52 (3H, s, H-15′), 1.40 (3H, s, ketal), 1.27 (3H, s, H-17′).

Ketal Formation of Sargachromanol E (5). Prepared as described for compound **4**. From 3.3 mg of **5** was obtained 2.1 mg of the cyclic ketal (**18**): ^{1}H NMR ($CDCl_3$) δ 6.48 (1H, d, J = 2.7 Hz, H-7), 6.39 (1H, d, J = 2.7 Hz, H-5), 5.48 (1H, t, J = 6.8 Hz, H-7′), 5.15 (1H, d, J = 8.6 Hz, H-11′), 5.13 (1H, t, J = 7.1 Hz, H-3′), 4.45 (1H, dd, J = 8.6, 8.6 Hz, H-10′), 3.96 (1H, d, J = 8.6 Hz, H-9′), 2.69 (2H, m, H-4), 2.13 (3H, s, H-18′), 2.12 (2H, m, H-2′), 2.10 (2H, m, H-6′), 1.98 (2H, t, J = 7.6 Hz, H-5′), 1.78 (1H, dt, J = 13.2, 6.8 Hz, H-3), 1.74 (3H, s, H-13′), 1.73 (1H, m, H-3), 1.65 (3H, s, H-15′), 1.64 (3H, s, H-14′), 1.62 (1H, m, H-1′), 1.58 (3H, s, H-16′), 1.54 (1H, m, H-1′), 1.45 (3H, s, ketal), 1.43 (3H, s, ketal), 1.26 (3H, s, H-17′).

MTPA Esterification of Sargachromanol F (6). From 2.7 and 3.1 mg of compound **6** were obtained 2.4 and 2.0 mg of (*S*)- and (*R*)-MTPA ester, **6S** and **6R**, respectively. **6S**: ^{1}H NMR ($CDCl_3$) δ 7.66−7.27 (phenyl), 6.723 (H-7), 6.685 (H-5), 5.467 (H-7′), 5.376 (H-9′), 5.131 (H-3′), 5.080 (H-11′), 4.070 (H-10′), 3.743 (OCH_3), 3.633 (OCH_3), 3.244 (9′-OCH_3), 2.754 (H-4), 2.181 (H-18′), 2.133 (H-2′), 2.113 (H-6′), 2.099 (H-5′), 1.755 (H-13′), 1.646 (H-14′), 1.598 (H-16′), 1.538 (H-15′), 1.269 (H-17′). **6R**: ^{1}H NMR ($CDCl_3$) δ 7.65−7.33 (phenyl), 6.711 (H-7), 6.673 (H-5), 5.586 (H-7′), 5.393 (H-9′), 5.132 (H-3′), 4.952 (H-11′), 4.022 (H-10′), 3.674 (OCH_3), 3.494 (OCH_3), 3.187 (9′-OCH_3), 2.744 (H-4), 2.170 (H-18′), 2.156 (H-6′), 2.134 (H-2′), 2.119 (H-5′), 1.668 (H-15′), 1.658 (H-13′), 1.595 (H-16′), 1.526 (H-14′), 1.268 (H-17′). $\Delta\delta$(**6S**−**6R**) H-4, +0.010 ppm; H-5, +0.012 ppm; H-7, +0.012 ppm; H-2′, −0.001 ppm; H-3′, −0.001 ppm; H-5′, −0.020 ppm; H-6′, −0.043 ppm; H-7′, −0.119 ppm; H-9′, −0.017 ppm; H-10′, +0.048 ppm; H-11′, +0.128 ppm; H-13′, +0.097 ppm; H-14′, +0.120 ppm; H-15′, −0.130 ppm;

H-16′, +0.003 ppm; H-17′, +0.001 ppm; H-18′, +0.011 ppm; 9′-OCH_3, +0.057 ppm.

MTPA Esterification of Sargachromanol G (7). From 2.1 and 2.5 mg of compound **7** were obtained 1.9 and 2.0 mg of (*S*)- and (*R*)-MTPA ester, **7S** and **7R**, respectively. **7S**: ^{1}H NMR ($CDCl_3$) δ 7.64−7.40 (phenyl), 6.715 (H-7), 6.673 (H-5), 6.563 (H-7′), 6.376 (H-10′), 5.243 (H-11′), 5.157 (H-3′), 3.677 (OCH_3), 3.536 (OCH_3), 2.745 (H-4), 2.326 (H-6′), 2.158 (H-18′), 2.119 (H-2′), 2.095 (H-5′), 1.801 (H-14′), 1.791 (H-15′), 1.777 (H-13′), 1.612 (H-16′), 1.278 (H-17′). **7R**: ^{1}H NMR ($CDCl_3$) δ 7.64−7.39 (phenyl), 6.718 (H-7), 6.675 (H-5), 6.587 (H-7′), 6.365 (H-10′), 5.186 (H-11′), 5.153 (H-3′), 3.688 (OCH_3), 3.676 (OCH_3), 2.749 (H-4), 2.353 (H-6′), 2.159 (H-18′), 2.133 (H-2′), 2.110 (H-5′), 1.813 (H-15′), 1.718 (H-14′), 1.689 (H-13′), 1.617 (H-16′), 1.278 (H-17′). $\Delta\delta$(**7S**−**7R**) H-4, −0.004 ppm; H-5, −0.002 ppm; H-7, −0.003 ppm; H-2′, −0.014 ppm; H-3′, +0.004 ppm; H-5′, −0.015 ppm; H-6′, −0.027 ppm; H-7′, −0.024 ppm; H-10′, +0.011 ppm; H-11′, +0.057 ppm; H-13′, +0.088 ppm; H-14′, +0.083 ppm; H-15′, −0.022 ppm; H-16′, −0.005 ppm; H-17′, 0 ppm; H-18′, −0.001 ppm.

MTPA Esterification of Sargachromanol H (8). From 1.5 and 1.5 mg of **8** were obtained 1.1 and 1.3 mg of (*S*)- and (*R*)-MTPA ester, **8S** and **8R**, respectively. **8S**: ^{1}H NMR ($CDCl_3$) δ 7.65−7.39 (phenyl), 6.710 (H-7), 6.678 (H-5), 5.958 (H-10′), 5.562 (H-6′), 5.415 (H-7′), 5.184 (H-3′), 5.182 (H-11′), 3.673 (OCH_3), 3.542 (OCH_3), 3.411 (H-8′), 2.751 (H-4), 2.156 (H-18′), 1.814 (H-14′), 1.790 (H-13′), 1.596 (H-16′), 1.273 (H-17′), 1.107 (H-15′). **8R**: ^{1}H NMR ($CDCl_3$) δ 7.63−7.38 (phenyl), 6.713 (H-7), 6.679 (H-5), 5.962 (H-10′), 5.591 (H-6′), 5.447 (H-7′), 5.200 (H-3′), 5.112 (H-11′), 3.672 (OCH_3), 3.542 (OCH_3), 3.423 (H-8′), 2.753 (H-4), 2.158 (H-18′), 1.759 (H-14′), 1.707 (H-13′), 1.609 (H-16′), 1.278 (H-17′), 1.136 (H-15′). $\Delta\delta$(**8S**−**8R**) H-4, −0.002 ppm; H-5, −0.001 ppm; H-7, −0.003 ppm; H-3′, −0.016 ppm; H-6′, −0.029 ppm; H-7′, −0.032 ppm; H-8′, −0.012 ppm; H-10′, −0.004 ppm; H-11′, +0.070 ppm; H-13′, +0.083 ppm; H-14′, +0.055 ppm; H-15′, −0.029 ppm; H-16′, −0.013 ppm; H-17′, −0.005 ppm; H-18′, −0.002 ppm.

MTPA Esterification of Sargachromanol I (9). From 1.9 and 2.2 mg of compound **9** were obtained 1.5 and 1.9 mg of (*S*)- and (*R*)-MTPA ester, **9S** and **9R**, respectively. **9S**: ^{1}H NMR ($CDCl_3$) δ 7.64−7.57 (phenyl), 7.48−7.41 (phenyl), 6.714 (H-7), 6.671 (H-5), 5.951 (H-10′), 5.210 (H-11′), 5.115 (H-3′), 3.677 (OCH_3), 3.548 (OCH_3), 2.738 (H-4), 2.634 (H-8′), 2.157 (H-18′), 2.126 (H-2′), 1.943 (H-5′), 1.851 (H-14′), 1.826 (H-13′), 1.630 (H-1′), 1.570 (H-16′), 1.535 (H-1′), 1.361 (H-6′), 1.274 (H-17′), 1.010 (H-15′). **9R**: ^{1}H NMR ($CDCl_3$) δ 7.64−7.56 (phenyl), 7.48−7.41 (phenyl), 6.715 (H-7), 6.672 (H-5), 5.929 (H-10′), 5.154 (H-11′), 5.122 (H-3′), 3.671 (OCH_3), 3.545 (OCH_3), 2.745 (H-4), 2.664 (H-8′), 2.159 (H-18′), 2.135 (H-2′), 1.966 (H-5′), 1.781 (H-14′), 1.777 (H-13′), 1.638 (H-1′), 1.578 (H-16′), 1.545 (H-1′), 1.401 (H-6′), 1.276 (H-17′), 1.048 (H-15′). $\Delta\delta$(**9S**−**9R**) H-4, −0.007 ppm; H-5, −0.001 ppm; H-7, −0.001 ppm; H-1′, −0.010, −0.008 ppm; H-2′, −0.009 ppm; H-3′, −0.007 ppm; H-5′, −0.023 ppm; H-6′, −0.040 ppm; H-8′, −0.030 ppm; H-10′, +0.022 ppm; H-11′, +0.056 ppm; H-13′, +0.049 ppm; H-14′, +0.070 ppm; H-15′, −0.038 ppm; H-16′, −0.008 ppm; H-17′, −0.002 ppm; H-18′, −0.002 ppm.

MTPA Esterification of Sargachromanol J (10). From 1.3 and 1.3 mg of compound **10** were obtained 1.2 and 0.9 mg of (*S*)- and (*R*)-MTPA ester, **10S** and **10R**, respectively. **10S**: ^{1}H NMR ($CDCl_3$) δ 7.65−7.55 (phenyl), 7.46−7.41 (phenyl), 6.714 (H-7), 6.672 (H-5), 5.262 (H-10′), 5.110 (H-3′), 3.674 (OCH_3), 3.648 (OCH_3), 2.742 (H-4), 2.657 (H-8′), 2.156 (H-18′), 2.127 (H-2′), 1.922 (H-5′), 1.564 (H-16′), 1.534 (H-12′), 1.504 (H-11′), 1.461 (H-11′), 1.277 (H-17′), 1.212 (H-15′), 0.840 (H-14′), 0.836 (H-13′). **10R**: ^{1}H NMR ($CDCl_3$) δ 7.64−7.57 (phenyl), 7.46−7.41 (phenyl), 6.713 (H-7), 6.672 (H-5), 5.287 (H-10′), 5.104 (H-3′), 3.676 (OCH_3), 3.553 (OCH_3), 2.743 (H-4), 2.629 (H-8′), 2.156 (H-18′), 2.125 (H-2′), 1.906 (H-5′), 1.800 (H-12′), 1.628 (H-11′), 1.559 (H-16′), 1.274 (H-17′), 1.164 (H-15′), 0.959 (H-14′), 0.951 (H-13′). $\Delta\delta$(**10S**−**10R**) H-4, −0.001 ppm; H-5, 0 ppm; H-7, +0.001 ppm; H-2′, +0.002 ppm; H-3′, +0.006 ppm; H-5′, +0.016 ppm; H-8′, +0.028 ppm; H-10′, −0.025 ppm; H-11′, −0.167, −0.124 ppm; H-12′, −0.266 ppm; H-13′, −0.155 ppm; H-14′, −0.119 ppm; H-15′, +0.048 ppm; H-16′, +0.005 ppm; H-17′, +0.003 ppm; H-18′, 0 ppm.

MTPA Esterification of Sargachromanol K (11). From 1.4 and 1.7 mg of compound **11** were obtained 1.2 and 1.7 mg of (*S*)- and (*R*)-MTPA ester, **11S** and **11R**, respectively. **11S**: ^{1}H NMR ($CDCl_3$) δ 7.64 (phenyl), 7.47−7.38 (phenyl), 6.706 (H-7), 6.678 (H-5), 6.128 (H-11′), 5.663 (H-7′), 5.543 (H-9′), 5.124 (H-3′), 3.675 (OCH_3), 3.667 (OCH_3), 2.745 (H-4), 2.189 (H-14′), 2.154 (H-18′), 1.904 (H-13′), 1.582 (H-16′), 1.503 (H-15′), 1.275 (H-17′). **11R**: ^{1}H NMR ($CDCl_3$) δ 7.64 (phenyl), 7.48−7.36 (phenyl), 6.709 (H-7), 6.677 (H-5), 6.078 (H-11′), 5.728 (H-7′), 5.550 (H-9′), 5.145 (H-3′), 3.676 (OCH_3), 3.572 (OCH_3), 2.745 (H-4), 2.168 (H-14′), 2.156 (H-18′), 1.872 (H-13′), 1.604 (H-16′), 1.577 (H-15′), 1.272 (H-17′). $\Delta\delta$(**11S**−**11R**) H-4, 0 ppm; H-5, 0 ppm; H-7, −0.003 ppm; H-3′, −0.021 ppm; H-7′, −0.065 ppm; H-9′, −0.007 ppm; H-11′, +0.050 ppm; H-13′, +0.032 ppm; H-14′, +0.021 ppm; H-15′, −0.074 ppm; H-16′, −0.022 ppm; H-17′, +0.003 ppm; H-18′, −0.002 ppm.

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