New Erythrolides from the Caribbean Gorgonian Octocoral *Erythropodium caribaeorum*

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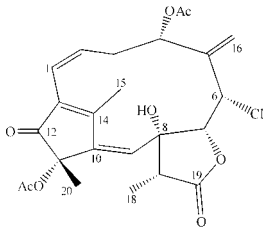
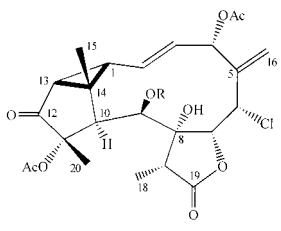
Seven new briarane diterpenes, erythrolides K−Q (**1**−**7**), as well as the known compounds erythrolides A, B, C, F, and J have been isolated from samples of the Caribbean gorgonian *Erythropodium caribaeorum* collected at Buccoo Reef and Flying Reef, Tobago. The structures of the new compounds were determined by high-resolution ^{1}H and ^{13}C NMR spectroscopy utilizing COSY, HMBC, HMQC, and NOESY experiments. The structures of erythrolides K and P were confirmed and their relative stereochemistry determined by X-ray crystallographic analysis.

Previous chemical investigations of *Erythropodium caribaeorum* have yielded 13 compounds possessing the briarane skeleton, viz., erythrolides A−J,[1−3] and acetate analogues of E, F, and H,[4] as well as the sesquiterpene erythrodiene.[5] In our continuing investigation of this organism, a sample collected at Eastern Reef, Buccoo, Tobago, yielded an unusual diterpene, erythrolide K, **1**, containing a rare [9.2.1] bicycloskeleton, whose structure we reported earlier as well as its derivatization from erythrolide A by a thermal conversion.[6]

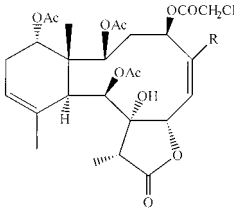
From this same sample of the organism, we now report the isolation of erythrolide K as well as the isolation and structural elucidation of six additional novel erythrolides, L−Q, **2**−**7**, and the identification of the known compounds erythrolides A, B, F, and J. Erythrolides A, B, C, F, J, K, and M are also reported from an *E. caribaeorum* sample collected at Flying Reef, Tobago. The erythrolides were isolated by conventional methods as outlined in the Experimental Section. The known compounds were identified by comparison of their physical properties and spectral data with those reported in the literature.[1−3]



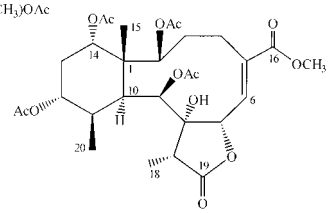
Erythrolide K (1)



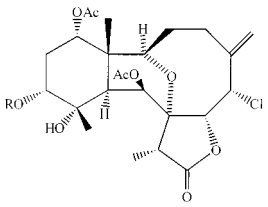
Erythrolide L (2) : R = $COCH_2OC(O)CH_3$



Erythrolide M (3) : R = CH_3
Erythrolide N (4) : R = CH_2OH



Erythrolide O (5)



Erythrolide P (6) : R = H
Erythrolide Q (7) : R = Ac

Results and Discussion

Compound **1**, erythrolide K, is the first briarein diterpene isolated possessing an unusual bicyclo [9.2.1] tetradecane skeleton. Its structure was solved by single-crystal X-ray structure analysis, and the structure of this compound as well as its two-step synthesis from erythrolide A was recently published.[6]

Compound **2**, erythrolide L, was isolated from a fraction that was slightly more polar than the fraction containing erythrolides A and B. A molecular formula, $C_{28}H_{33}O_{12}Cl$, derived from ^{1}H and ^{13}C data, was confirmed by high-resolution EIMS ([M^+] *m*/*z* 596.1638). This molecular formula contained two carbon, two hydrogen, and two oxygen atoms more than that for erythrolide A. The IR spectrum (Nujol) showed stretching frequencies at 3480, 1775, and 1740 cm $^{-1}$, which were consistent with the presence of hydroxyl, γ-lactone, and ester carbonyl functionalities, respectively. Inspection of the ^{1}H and ^{13}C spectral data showed that all the ^{13}C and ^{1}H resonances present in erythrolide A could be identified in this compound. The additional two protons present in compound **2** were present as an AB system centered at δ_H 4.72 (d, J = 14.1 Hz) and 4.75 (d, J = 14.1 Hz). In addition, the H-9 proton signal at δ_H 5.45 (d, J = 2.0 Hz) in erythrolide A now appeared at δ_H 5.54 (d, J = 1.8 Hz). The additional carbon resonances were at δ_C 168.7 and 60.7. These NMR data suggested the presence of an acetoxyacetate group, [−OC(O)CH_2OC(O)CH_3], in erythrolide L. Further evidence for this functionality came from the low-resolution mass spectral data of erythrolide L, which showed a base peak at *m*/*z* 101 corresponding to the ion fragment $^+$O≡CCH_2-OC(O)CH_3. The site of attachment of this functionality to the main skeleton at C-9 was determined by HMBC data. The carbonyl resonance at δ_C 168.7 (C-1′ of the acetoxyacetyl group) showed HMBC correlations with both H-9 (δ_H, 5.54) and the methylene protons of the AB system. The

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latter protons were also coupled with the acetate carbonyl carbon (C-3′) at δ_C 169.8. Erythrolide L was thus established to be the C-9 acetoxyacetate analogue of erythrolide A. The direct connectivities from C-1 to C-14 and through to C-17 as well as the relationship of the latter to C-18 and C-19 were established by the use of ^{1}H and ^{1}H−^{1}H COSY and ^{13}C, HMBC, and HMQC data. The stereochemistry of compound **2** was established by spectral comparisons with erythrolide A.[1] The shapes of H-1 to H-4, H-6, H-7, H-9, H-10, H-13, H-17, and H-18 signals of compound **2** were very similar to those of erythrolide A.

Compound **3**, erythrolide M, was isolated as a colorless gum. The molecular formula, $C_{32}H_{44}O_{13}$, was established from the high-resolution EIMS data. Like **2**, compound **3** showed IR stretching frequencies at 3450, 1775, and 1735 cm^{-1}, indicating hydroxyl, γ-lactone, and ester carbonyl functionalities, respectively. The ^{13}C NMR data revealed the presence of (a) six ester or lactone carbonyl carbons (δ_C 175.9, 171.0, 170.4, 170.1, 169.7, and 169.3); (b) four sp^2 carbon atoms (δ_C 145.6, 134.3, 122.4, and 120.8); (c) seven sp^3 oxygenated carbon atoms (δ_C 81.6, 77.5, 73.2, 72.6, 72.5, 69.3, and 66.9); (d) one quaternary carbon signal (δ_C 44.8); (e) two methine carbon signals (δ_C 43.6 and 39.8); (f) three methylene carbon signals (δ_C 41.2, 37.7, and 26.4); and (g) in the high-field region, nine methyl carbon signals (δ_C 25.8−6.9). The above signals account for the 32 carbon and 13 oxygen atoms (six carbonyl and seven C−O groups) required by the molecular formula.

Analysis of the ^{1}H NMR spectrum suggested that four of the nine methyl groups were attributable to acetate moieties (CH_3CO) occurring as sharp singlets at δ_H 2.24, 2.03, 2.02, and 1.95, and each integrating for three protons. Three of the five remaining methyl groups were doublets at δ_H 2.19, 1.28, and 1.26, while the other two methyl groups were singlets at δ_H 1.98 and 0.98. From biogenetic analogy, the briarane nucleus would accommodate a maximum of four C-methyl groups, located at C-15, C-16, C-18, and C-20. The presence of five C-methyl groups in the above compound suggests a methyl group attached to a side chain. Further analysis of the ^{1}H NMR spectrum revealed the presence of a 3-acetoxybutanoyl moiety indicated by the following signals: (a) an AB pair of doublets at δ_H 2.52 (J = 15.1, 5.3 Hz) and 2.65 (J = 15.1, 8.0 Hz); and (b) a multiplet at δ_H 5.28. The presence of this functionality was further supported by a fragment ion corresponding to (MH^+ − 145) and COSY, HMBC, and HMQC data. To date, only one other briarane compound, erythrolide J, has been reported to possess a 3-acetoxybutanoyl substituent.[3]

Comparison of the ^{1}H NMR spectrum of this compound with that of erythrolide J revealed the following major differences: (a) the presence of four acetate methyl signals compared with five in erythrolide J, and five C-methyl groups compared with four in erythrolide J; and (b) the absence of a three-proton singlet characteristic of an −OMe group as found in erythrolide J. The 3-acetoxybutanoyl substituent was placed at position C-4 since its carbonyl carbon (C-1′ of the 3-acetoxybutanoyl group) at δ_C 169.7 showed HMBC correlation to the proton at δ_H 5.08 (H-4) and the methylene protons at δ_H 2.52 and 2.65. The acetate groups on the main skeleton were placed at positions C-2, C-9, and C-14 and two of the C-methyl groups on olefinic carbons at C-6 and C-11 based on appropriate HMBC correlations.

The relative stereochemistry of compound **3** was deduced from NOESY data (Table 3). Assignment of the ring junction methyl (C-15) on the β-face of the molecule by analogy with other briaranes places H-14 on the β-face as well. NOESY correlation between the H-2 and H-10 protons together with the lack of NOESY correlation between H-2 and the β-assigned H-15 methyl signal was consistent with the trans ring junction and the H-10 and H-15 protons being on opposite faces of the molecule. NOESY correlation between H-9 and H-10 placed H-9 on the α-face of the molecule. Similar correlation between the C-8 hydroxyl proton and H-10 places the former on the α face of the molecule, and its further correlation with the C-18 methyl signal locates the latter also on the α face and H-17, as a consequence, on the β face. H-7 is deduced to be β due to NOESY correlation between it and H-17. Correlation of H-9 with both H-18 and H-17 indicates its close spacial proximity to both H-17 and the C-18 methyl group and is consistent with a β-oriented C-9 acetate group. The large coupling between the vinyl proton H-6 and the oxymethine proton at H-7 (J = 9.6 Hz) suggests an antiparallel orientation of these protons; thus H-6 and H-7 must be directed toward opposite faces of the molecule. The relative stereochemistry at C-4 was based on that of the closely related compound **4**, erythrolide N. In the latter molecule, NOESY correlation indicated an α-orientation for the H-4 proton. The position and shape of the resonance signal of the H-4 proton in both compounds **3** and **4** was almost the same (Table 2), thus allowing us to attribute an α orientation to this proton in erythrolide M, **3**.

Compound **4**, erythrolide N, was isolated as a colorless gum, and high-resolution EIMS established the molecular

Table 1. ^{13}C NMR Assignments of Compounds **2**−**7**[a]

position	**2**	**3**	**4**	**5**	**6**	**7**
1	37.4	44.8	44.8	45.2	41.1	40.7
2	127.0	72.6	73.7	74.5	78.6	78.8
3	133.1	37.7	37.6	30.5	29.4	29.3
4	75.6	72.5	71.1	22.8	31.3	31.5
5	138.4	145.6	146.7	139.4	142.5	142.4
6	59.6	122.4	126.2	132.8	57.9	57.2
7	80.6	77.5	77.3	77.4	84.4	84.5
8	83.0	81.6	81.7	83.2	83.2	83.5
9	81.7	69.3	69.5	76.2	71.9	71.5
10	43.9	39.8	39.7	34.2	38.0	38.2
11	87.3	134.3	134.5	42.6	71.1	70.8
12	204.5	120.8	120.4	72.7	74.0	75.0
13	39.7	26.4	26.3	24.8	30.4	28.6
14	28.6	73.2	73.1	74.7	76.8	75.8
15	22.6	14.5	14.4	15.3	19.0	18.9
16	127.6	25.8	67.0	168.9	117.9	118.0
17	43.7	43.6	43.7	43.6	47.5	47.6
18	9.6	6.9	6.9	6.6	9.0	8.5
19	174.8	175.9	176.0	175.4	175.3	175.3
20	21.7	24.6	27.5	15.2	23.1	24.4
C-2 ester		170.4	171.9	170.3		
		21.1	21.2	21.0		
C-4 ester	167.7	169.7	169.7			
	20.9	169.3	169.6			
		66.9	66.9			
		41.2	41.2			
		21.5	21.5			
		20.1	20.1			
C-9 ester	169.8	170.1	170.2	169.4	169.5	169.5
	168.7	21.2	21.2	21.7	21.4	21.4
	60.7					
	20.3					
C-11 ester	169.7					
	21.1					
C-12 ester				170.5		170.8
				21.4		21.1
C-14 ester		171.0	171.0	169.0	170.2	170.6
		21.4	21.2	21.3	21.5	21.4
-OMe				52.6		

[a] Spectra were recorded in $CDCl_3$ on a Varian Unity 500 spectrometer at 125 MHz with TMS as an internal standard. All assignments were based on HMBC and HMQC experiments.

Table 2. ^{1}H NMR Assignments of Compounds **2**−**7**[a]

position	2	3	4	5	6	7
1	2.33 (10.4,7.1)					
2	6.48 (16.7, 7.1, 1.5)	4.86 (7.5)	4.84 (7.6)	5.05 (8.2)	3.85 (13.0, 4.9)	3.90 (13.3, 4.8)
3	5.88 (16.7, 1.5)	1.94 (m)	1.97 (m)	1.65 (m)	1.79 (m)	1.76 (m)
		2.94 (15.0, 12.8)	3.01 (15.3, 13.1)	2.68 (m)	2.26 (m)	2.28 (m)
4	6.02 (bs)	5.08 (12.8, 5.5, 1.6)	5.04 (13.1, 5.1, 0.6)	2.57 (m)	2.40 (m)	2.40 (m)
				2.68 (m)	2.64 (m)	2.65 (m)
6	4.56 (9.5)	5.54 (dt, 1.6, 9.6)	5.92 (10.3, 0.6)	6.64 (10.1, 2.2)	4.88 (1.9)	4.87 (2.0)
7	5.17 (9.5)	5.66 (9.6)	5.65 (10.3)	5.25 (10.1)	4.48 (1.9)	4.46 (2.0)
9	5.54 (1.8)	6.04 (2.0)	6.05 (2.6)	5.25 (1.6)	5.97 (bs)	5.96 (bs)
10	3.00 (bs)	2.83 (bs)	2.98 (bs)	2.85 (5.3)	2.46 (bs)	2.61 (bs)
11				1.99 (m)		
12		5.54 (bd)	5.44 (bd)	4.81 (m)	3.65 (m)	4.88 (m)
13	1.98 (10.4)	2.00 (m)	1.98 (m)	1.99 (m)	2.19 (m)	2.18 (m)
		2.24 (m)	2.25 (m)			
14		4.77 (bs)	4.80 (bs)	4.76 (t, 3.1)	4.70 (t, 3.4)	4.56 (t, 3.2)
15	1.55 (s)	0.98 (s)	0.98 (s)	1.18 (s)	1.24 (s)	1.26 (s)
16	5.50 (s)	2.19 (1.6)	4.43 (15.0, 7.6)		5.19 (bs)	5.19 (bs)
	5.64 (bs)				5.44 (bs)	5.43 (bs)
17	3.14 (q, 7.1)	2.55 (q, 7.1)	2.52 (q, 7.4)	2.52 (m)	2.75 (q, 7.3)	2.74 (q, 7.2)
18	1.25 (7.0)	1.26 (7.1)	1.26 (7.4)	1.25 (7.9)	1.37 (7.3)	1.42 (7.2)
20	1.40 (s)	1.98 (bs)	1.99 (bs)	1.12 (7.4)	1.25 (s)	1.30 (s)
8-OH	3.23 (bs)	2.36 (s)	3.64 (s)	3.75 (s)		
16-OH			3.70 (7.6, 5.1)			
C-2 ester		2.03 (s)	2.07 (s)	1.94 (s)		
C-4 ester	2.01 (s)	1.28 (6.3)	1.27 (6.3)			
		2.24 (s)	2.25 (s)			
		2.52 (15.1, 5.3)	2.51 (16.1, 5.0)			
		2.65 (15.1, 8.0)	2.64 (16.1, 8.0)			
		5.28 (m)	5.27 (m)			
C-9 ester	2.20 (s)	2.02 (s)	1.93 (s)	2.23 (s)	2.13 (s)	2.24 (s)
	4.72 (14.1)					
	4.75 (14.1)					
C-11 ester	2.15 (s)					
C-12 ester				2.05 (s)		2.07 (s)
C-14 ester		1.95 (s)	2.09 (s)	1.95 (s)	2.25 (s)	2.11 (s)
−OMe				3.82 (s)		

[a] Spectra were recorded at 500 MHz in $CDCl_3$ with TMS as an internal standard. All assignments were based on COSY, HMBC, and HMQC experiments with coupling constants (Hz) in parentheses. When multiplicity is not noted, a doublet is implied.

Table 3. NOESY Correlations for Compounds **2**−**4**, **6**, and **7**[a]

	NOESY correlations				
proton	2	3	4	6	7
H-2		H10	H10, H4	H14	H14
H-7	H17, H6	H17, H6	H17, H6	H17, H9, H6	H9, H6
H-9	H10	H18, H17, H10	H18, H17, H10	H20, H17, H10	H17, H10
H-14		H15	H15	H15	H15
H-15	H17, H13, H1	H3	H13	H20	
8-OH	H18, H6	H18, H10	H18, H10, H6		
H-20	H15		H12	H12	H12

[a] Spectra were recorded at room temperature in $CDCl_3$ solutions.

formula, $C_{32}H_{44}O_{14}$, indicating one oxygen atom more than the molecular formula for compound **3**. Like compound **3**, it showed IR absorptions at 3440, 1775, and 1730 cm^{-1} and an almost identical ^{1}H NMR spectrum. The significant differences were (a) the replacement of the H-16 vinyl methyl group (3H, d, J = 1.6 Hz) in compound **3** by two new proton signals at δ_H 4.43 (1H, dd, J = 15.0, 7.6 Hz) and 4.29 (1H, dd, J = 15.0, 5.1 Hz); (b) the presence of an additional hydroxyl group in compound **4** indicated by proton signals at δ_H 3.64 (s) and 3.70 (dd, J = 7.6, 5.1 Hz), which both disappeared on shaking with D_2O; and (c) a proton signal at δ_H 5.92 (dd, J = 10.3, 0.6 Hz), which replaced the H-6 signal of erythrolide M (δ_H 5.54, dt, J = 1.6, 9.6 Hz).

Comparison of the ^{13}C NMR spectrum of compounds **3** and **4** revealed the following major differences: (a) the loss of a carbon signal at δ_C 25.8 in compound **3** and the appearance of a new signal at δ_C 67.0 in compound **4**; and (b) the replacement of the carbon signal at δ_C 122.4 (C-6) in compound **3** with one at δ_C 126.2 in **4**. The above ^{1}H and ^{13}C NMR data are consistent with the replacement of the vinyl methyl group at C-16 in **3** by a −CH_2OH moiety in **4**. The methylene protons of the C-16 primary alcohol could be identified as those at δ_H 4.43 (dd, J = 15.0, 7.6 Hz) and 4.29 (dd, J = 15.0, 5.1 Hz) with the expected large geminal coupling (J = 15.0 Hz) between them. In addition, these two protons (at δ_H 4.43 and 4.29) showed further coupling to the hydroxyl proton at δ_H 3.70 (dd, J = 7.6, 5.1 Hz). From the COSY, HMQC, and HMBC data, the direct connectivities from C-1 to C-14 as well as the location of the carbons in the lactone ring (C-17, C-18, and C-19) were readily apparent. The ^{1}H NMR spectra of **3** and **4** revealed the similarity in both the shapes and positions of the proton signals for H-2, H-7, H-9, H-10, H-14, and H-17 in these two compounds. The stereochemistry at C-4 was determined from the NOESY data. In this compound correlation between H-2 and H-4 was observed. H-2 was assigned an α configuration in **3**. It follows that H-4 must also be on

the same face and thus in the α configuration. This assignment of the H-2 and H-4 protons on the α face of the molecule is the same as that reported for the known compound erythrolide J.

Compound **5**, erythrolide O, was isolated as a colorless gum, and HREIMS revealed an exact mass of 596.2478, consistent with a molecular formula $C_{29}H_{40}O_{13}$ (calc 596.2457). This compound revealed IR signals similar to those of erythrolides J, M, and N with stretching frequencies at 3550, 1775, and 1735 cm^{-1} assignable to hydroxyl, γ-lactone, and ester functionalities, respectively. In addition, the UV spectrum (MeOH) showed λ_{max} 216 nm (ϵ = 4600), indicating conjugation. Analysis of the ^1H NMR spectrum of **5** revealed the following: (a) four acetate groups indicated by sharp methyl singlets at δ_H 2.23, 2.05, 1.95, and 1.94; (b) three methyl groups in the high-field region at δ_H 1.25, (3H, d, J = 7.9 Hz), 1.18 (3H, s), and 1.12 (3H, d, J = 7.4 Hz); (c) one −OMe group indicated by a signal at δ_H 3.82 (3H, s); and (d) an AX system at δ_H 6.64 (dd, J = 10.1, 2.2 Hz) and 5.25 (d, J = 10.1 Hz), which could be assigned to the H-6 and H-7 protons, respectively. IR data indicated that the γ-lactone ring was intact. Thus, the presence of the −OMe group must be due to some other modification on the briarane skeleton. To date, two reported briarane compounds have been isolated that possess a −COOMe moiety together with an intact lactone ring. These compounds are stylatulide methyl ester[7,8] and erythrolide J.[3]

Inspection of the ^1H NMR spectrum of **5** indicated a very close similarity with that of erythrolide J. However this compound, unlike erythrolide J, showed no evidence of an acetoxybutanoyl substitutent and the corresponding oxymethine proton signal located at C-4 in erythrolide J. Instead, two new methylene proton signals at δ_H 2.57(m) and 2.68-(m) were observed. The above information is consistent with the absence of an acetoxybutanoate moiety at C-4 as in erythrolide J. The complete structure of **5** was revealed by analysis of the high-resolution and 2D NMR data. The relative stereochemistry of **5** at all asymmetric carbons was the same as in erythrolide J, whose stereochemistry was established by NOE difference experiments.[3] These assignments were based on the similarity of the shapes and positions of protons at C-2, C-6, C-7, C-9, C-10, C-14, C-17, and C-18 in both compounds.

Compound **6**, erythrolide P, was isolated as colorless crystals from the most polar fraction of the ethyl acetate extract. High-resolution EIMS established a molecular formula of $C_{24}H_{33}O_9Cl$ for this compound. The UV spectrum (MeOH) showed only end absoption at 208 nm. The IR spectrum revealed absorptions characteristic of hydroxyl groups (3520, 3350, and 3280 cm^{-1}), γ-lactone (1790 cm^{-1}), ester carbonyl (1750 cm^{-1}), and an sp^2 system (1695 cm^{-1}). The complete assignment of the ^1H NMR and ^{13}C NMR spectra for compound **6** was achieved by a combination of DEPT, COSY, HMBC, and HMQC data. Analysis of the ^1H NMR spectrum suggested that two of the five methyl groups were due to acetate moieties. They occurred at δ_H 2.13(s) and 2.25(s), and each integrated for three protons. Two of the three remaining methyl groups were singlets at δ_H 1.24 (C-15) and 1.25 (C-20), while the third methyl group was a doublet centered at δ_H 1.37 (C-18, J = 7.3 Hz). The ^{13}C NMR data revealed the presence of (a) three ester carbonyl carbons (δ_C 169.5−175.3); (b) two sp^2 carbon atoms at δ_C 142.5 and 117.9; (c) seven sp^3 oxygenated carbon atoms (δ_C 71.1−84.4); (d) two methine carbon signals at δ_C 57.9 and 47.5; (e) one quaternary carbon signal at δ_C 41.1; and (f) nine carbon signals in the high-field region (δ_C 9.0−38.0), which were assigned to five methyls, three methylenes, and one methine carbon atom. The above accounts for 24 carbons, as required by the molecular formula, and four degrees of unsaturation. The other four degrees of unsaturation can be accounted for by a tetracyclic structure. A total of 10 oxygenated carbons (three carbonyl groups and seven C−O groups) and a molecular formula $C_{24}H_{33}O_9Cl$ suggest that one of the oxygen atoms was bonded to two carbons. Thus a C-2/C-8 ether bridge was proposed to accommodate the nine oxygen atoms and the eight degrees of unsaturation required by the molecular formula. Support for the presence of this ether bridge was achieved by HMBC correlation of H-2 and C-8. Compound **6** is thus an addition to the group of C-2−O−C-8 cyclized briaranes (erythrolides E, F, G, and I[2] and the acetate analogues of E and F[4]). The relative stereochemistry was deduced from the NOESY data (Table 3). This stereochemistry and the deduced structure were confirmed by X-ray crystallographic analysis of compound **6** (Figure 1).

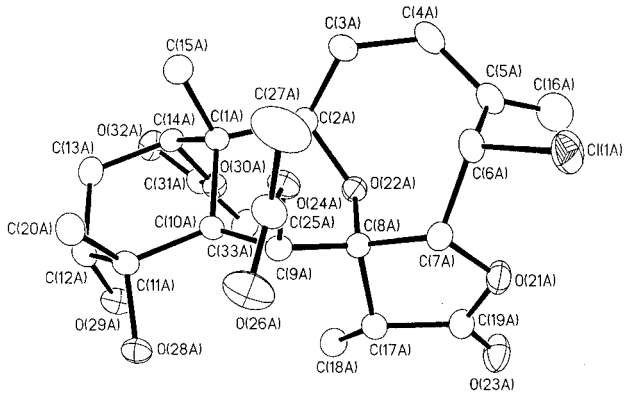

Figure 1. ORTEP drawing of erythrolide P (**6**).

Compound **7**, erythrolide Q, was shown to be the C-12 acetoxy analogue of compound **6**, on the basis of a comparison of the ^1H and ^{13}C NMR data of the two compounds. Thus, compound **7** showed NMR signals for three acetate moieties compared with two in compound **6**. The NMR signals for the additional acetate group were at δ_C 170.8 and 21.1 and δ_H 2.07 (s). In addition the C-12 and H-12 signals now appeared at δ_C 75.0 and δ_H 4.88 compared with δ_C 74.0 and δ_H 3.65 in compound **6**. The point of attachment of the acetate group was confirmed by HMBC correlation of its carbonyl signal at δ_C 170.8 with the H-12 signal at δ_H 4.88. The stereochemistry of **7** was established by spectral comparison with compound **6** and the NOESY data (Table 3). The ^1H and ^{13}C NMR spectra of **6** and **7** were virtually identical, and similar NOESY data were obtained for both molecules. Erythrolide Q is thus the 12-OAc analogue of erythrolide P. These two compounds are new members of the group of erythrolides possessing the C-2−O−C-8 ether bridge. Confirmation of this ether linkage in briarane compounds has now been established by the X-ray crystallographic analysis of compound **6**.

Experimental Section

General Experimental Procedures. The general experimental procedures and instrumentation used were as described previously[9] except for UV spectra, X-ray analysis, and HPLC analysis. UV spectra were recorded on a Hewlett-Packard HP 8452A photodiode array instrument and are for MeOH solutions. X-ray analysis was done using a Sheldrick, G. M. SHELXTL\PC, Siemens Analytical X-Ray Instrument. The HPLC system consisted of a reversed-phase SUPELCOSIL LC-18 analytical column (25.0 mm × 4.6 ID), a Gilson 307 piston pump, and a LDC/ Milton Roy Model 1107

refractive index detector with MeOH (AR Grade)/H_2O as solvent. All organic solvents used for chromatography were purified by distillation. Purifications were achieved by use of gravity column chromatography (CC), preparative TLC (PTLC), vacuum liquid chromatography (VLC), and high-performance liquid chromatography (HPLC).

Animal Material. Two collections of the gorgonian *Erythropodium caribaeorum* were made at Tobago on March 19, 1994, from Eastern Reef, Buccoo Reef (−6 m), and Flying Reef (−9 m), respectively. The samples were identified by Mr. Richard S. Laydoo, formerly of the Institute of Marine Affairs, Trinidad and Tobago. Voucher specimens have been deposited at the Institute (specimen nos. IMA-3010 and IMA-3011, respectively).

Extraction and Isolation. The extraction procedure was similar for both samples, and details are given for the sample collected at Eastern Reef, Buccoo Reef. Yields (%) of crude extracts or pure compounds are based on the dry weight of the extracted organism.

The sample was steeped in acetone and subsequently macerated and exhaustively extracted with Me_2CO. The extract was filtered and evaporated under reduced pressure to yield an aqueous suspension. The latter was extracted with EtOAc. The EtOAc extract was dried over anhydrous Na_2SO_4, filtered, and evaporated to give a dark brown gum (9.16 g, 7.8%). This gum was suspended in 90% aqueous MeOH and extracted sequentially with petroleum ether and EtOAc. The latter extract was dried over anhydrous Na_2SO_4 and evaporated to give a brown gum (5.44 g, 4.6%), which was subjected to CC using petroleum ether (60−80°) and increasing amounts of EtOAc to give 125 fractions (50 mL each), which were grouped into nine major fractions based on their TLC profile. The grouped fractions were purified via a combination of HPLC, PTLC, and crystallization to give the erythrolides in order of increasing polarity: M (9 mg, 0.01%), K (2.5 mg, 0.02%), B (1.74 g, 1.48%), A (364 mg, 0.31% dry wt), L (15 mg, 0.01%), N (3.7 mg, 0.003%), J (82.1 mg, 0.07%), Q (2 mg, 0.002%), F (23.5 mg, 0.02%), O (5 mg, 0.004%), and P (8 mg, 0.01%).

For the sample of *E. caribaeorum* collected at Flying Reef, the final EtOAc extract (10.86 g, 6.1%) was immediately subjected to VLC (petroleum ether/EtOAc), and fractions were grouped and subjected to CC and PTLC in a manner similar to that for the first sample. Erythrolides A, B, F, J, K, and M were identified from fractions of similar polarity as before. In addition, erythrolide C (2 mg, 0.001%) was obtained from this sample. The known compounds were identified by comparison of their spectral and physical data with literature values.[1−3]

Erythrolide K (1): colorless crystals: mp 220° (dec) (petroleum ether/Me_2CO); $[\alpha]_D^{25}$ −50.0° (*c* 0.40, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 208 (3.93), 214 (3.92) and 296 (3.68) nm; IR ν_{max} (Nujol) 3450, 1785, 1745, 1710 cm^{-1}; EIMS (%) 478 (M^+, <1), 436 (22), 376 (83), 341 (36), 295 (55), 263 (45), 175 (100), 151 (47), 133 (43), 91 (36); HRMS *m*/*z* 478.1370 (calcd for $C_{24}H_{27}O_8Cl$, 478.1387).

Erythrolide L (2): colorless gum: $[\alpha]_D^{25}$ −62.9° (*c* 0.35, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 216 (3.94) nm; IR ν_{max} (Nujol) 3480, 1775, 1740 cm^{-1}; EIMS (%) 596 (M^+, <1), 562 (2), 536 (20), 496 (7), 459 (8), 376 (27), 341 (17), 277 (15), 177 (25), 101 (100), 73 (66), 57 (36); HRMS *m*/*z* 596.1638 (calcd for $C_{28}H_{33}O_{12}Cl$, 596.1651).

Erythrolide M (3): colorless gum: $[\alpha]_D^{25}$ +55.0° (*c* 0.40, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 208 nm (end absorption); IR ν_{max} (Nujol) 3450, 1775, 1735 cm^{-1}; EIMS (%) 637 ($M^+ + H$, <1), 517 (5), 457 (9), 370 (17), 328 (58), 310 (46), 254 (16), 227 (23), 211 (29); HRMS *m*/*z* 636.2780 (calcd for $C_{32}H_{44}O_{13}$, 636.2769).

Erythrolide N (4): colorless gum: $[\alpha]_D^{25}$ +20.0° (*c* 0.32, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 208 nm (end absorption); IR ν_{max} (Nujol) 3440, 1775, 1730 cm^{-1}; EIMS (%) 652 (M+, <1), 534 (20), 386 (8), 326 (24), 225 (36), 209 (48), 135 (18), 107 (42), 69 (100), 55 (20); HRMS *m*/*z* 652.2756 (calcd for $C_{32}H_{44}O_{14}$, 652.2718).

Erythrolide O (5): colorless gum: $[\alpha]_D^{25}$ +58.5° (*c* 0.41, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 216 (3.66) nm; IR ν_{max} (Nujol) 3550, 1775, 1735, 1700 cm^{-1}; EIMS (%) 596 (M^+, <1), 564 (2), 536 (11), 462 (21), 360 (48), 342 (57), 254 (82), 136 (66), 106 (100); HRMS *m*/*z* 596.2478 (calcd for $C_{29}H_{40}O_{13}$, 596.2457).

Erythrolide P (6): colorless crystals; mp 222.0−224.0° (petroleum ether/Me_2CO); $[\alpha]_D^{25}$ −16.0° (*c* 0.25, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 208 nm (end absorption); IR ν_{max} (Nujol) 3520, 3350, 3280, 1790, 1750, 1695 cm^{-1}; EIMS (%) 500 (M^+, 8), 483 (20), 465 (12), 441 (25), 425 (64), 407 (48), 389 (28), 369 (40), 345 (100); HRMS *m*/*z* 500.1790 (calcd for $C_{24}H_{33}O_9Cl$, 500.1804).

Erythrolide Q (7): colorless gum: $[\alpha]_D^{25}$ −20.0° (*c* 0.10, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 208 nm (end absorption); IR ν_{max} (Nujol) 3520, 3360, 3280, 1790, 1750, 1695 cm^{-1}; EIMS (%) 542 (M^+, 11), 499 (16), 485 (44), 465 (88), 387 (100), 327 (66), 109 (64); HRMS *m*/*z* 542.1919 (calcd for $C_{26}H_{35}O_{10}Cl$, 542.1909).

Single-Crystal X-ray Crystallography of Erythrolide P (6).[10] Suitable crystals were obtained from a solution in petroleum ether/acetone. The crystal (0.36 × 0.23 × 0.18 mm) belongs to the monoclinic system, space group $P2_1$ with a = 8.734(2) Å, b = 23.8531(14) Å, c = 12.1827(6) Å, β = 105.487(9)°, V = 2446.0(5) $Å^3$, Z = 8, D_{calcd} = 2.721 g/cm^3, λ(Mo Kα) = 0.71073 Å. Intensity data were measured on a Bruker P4 diffractometer up to 2θ = 57.18°. A total of 3679 reflections were collected, of which 3426 were unique. The structure was solved by direct methods and refined by the least-squares method (on F_o^2 using all unique data). Non-hydrogen atoms were assigned anisotropic displacement parameters, and hydrogen atoms were placed in calculated positions and treated as riding atoms. The refinement converged to give $R_1[F_o > 4\sigma(F_o)] = 0.0402$ and wR_2(all data) = 0.1099 for 641 parameters.

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Supporting Information Available: X-ray data for erythrolide P (**6**). This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) Crystallographic data for this structure have been deposited with the Cambridge Crystallographic Data Centre. A copy of the data can be obtained (CCDC 173531), free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)1223-336003 or e-mail: deposit@ccdc.cam.ac.uk).

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