Spirocaracolitone Triterpenoids from the Bark of *Ruptiliocarpon caracolito*

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Six new triterpenoids named spirocarcolitones (G−L), which belong to a novel class of CD-spiro triterpenoids, were isolated from the dichloromethane-soluble fraction of the bark of *Ruptiliocarpon caracolito.* The structures of these natural products were established using mainly 1D and 2D NMR spectroscopy. One known CD-spiro triterpenoid and canophyllol were also isolated from the same source.

Several years ago, we reported our initial phytochemical investigations of *Ruptiliocarpon caracolito*, a unique American species belonging to the family Lepidobotryaceae.[1,2] This species, which is endemic to the Osa peninsula of southwestern Costa Rica, belongs to one of only two genera of this family. The other is found in West Africa.[3] The EtOH extracts of the bark administered to insect diets were shown to be highly active as a growth reducer when tested against the European corn borer (*Orstrinia nubilalis* Hubner). Bioassay-guided fractionation led to the isolation of a series of six new triterpenes, which were named spirocaracolitones A−F.[1,2] These compounds were shown to have unprecedented CD-spiro structures, an uncommon oxidation pattern in ring A, and a γ-lactone ring connecting C-18 and an oxidized C-30 carbon. These features are illustrated by the structure of spirocaracolitone A, Figure 1. Variations in the structures of the derivatives A−D were due to different hydroxylation patterns in rings D and E and esterification of these hydroxy groups with different acyl groups, affording acetates, benzoates, and tiglates. In spirocaracolitones E and F, the C3−C4 bond in ring A had undergone oxidative cleavage to a dimethyl ester (Figure 3) The structures of spirocaracolitones A and E were confirmed by single-crystal X-ray diffraction.[2]

The rings A and B methyl group pattern indicated that these compounds belong to the friedelin family of triterpenes. A possible biogenetic pathway for the genesis of the spiro system was proposed involving generation of a C-12 carbocation in the friedelin skeleton, migration of the C-13 methyl group, thereby generating a new cation at C-13, followed by migration of the C-8−C-14 bond.[2] This sequence, shown in Scheme 1, accounts for the relative configuration of the ring junctions and methyl groups. Canophyllol,[4] a friedelin-type triterpene,[5] was also isolated from the same extracts.

All of these compounds were active as insect-growth reducers using the European corn borer as the test insect.[1] The bioassay studies also demonstrated synergism between the various analogues. The production of a number of closely related analogues of varying potency appears to be another example of phytochemical redundancy in chemical defenses, a strategy whereby the plant protects itself against an easy adaptation by the pest by becoming resistant to a single entity defense compound.[6]

Results and Discussion

In order to obtain access to additional quantities of these unusual compounds for further bioassays, we re-collected bark from a tree near Golfito, an area adjacent to the Osa peninsula. The earlier sample had been collected at the Marenco Biological Reserve, on the northwest coast of Osa. The distance between these two areas is approximately 50 km. Surprisingly, except for the parent compound spirocaracolitone A, none of the other spiro derivatives described earlier[2] could be isolated from the bark of this collection. However, we were able to isolate and identify six new spiro compounds, which we have designated as spirocaracolitones G−L. The structure elucidation of these new compounds was carried out mainly by a combination of 1D and 2D NMR spectroscopy and by comparison of these spectra with those of the known spirocaracolitones. Virtually all key proton and carbon resonances have been assigned for the new compounds. Complete ^{1}H, ^{13}C, COSY, HMQC, and HMBC NMR data for the six new compounds are listed in Tables 1 and 2. The reason for the differences observed between the collections could be due to seasonal variations or to different subspecies. Several new collections are being initiated to address this issue.

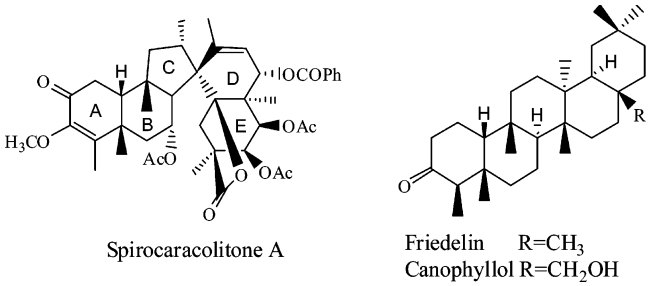

Figure 1.

The new spirocaracolitone derivatives G and H are closely related to spirocaracolitone A (Figure 2). Derivative G lacks the acetoxy group at C-21 compared to spirocaracolitone A. Spirocaracolitone H differs from G only in the replacement of the C-22 acetoxy group by a benzoyloxy substituent. These changes were highlighted by the appearance of an ABX spin system due to the −CH_2−CH−(OAc)− unit for C-21 and C-22. In contrast, spirocaracolitone A showed a pair of doublets due to the H-21 and H-22 methine hydrogens. The X-portion of the ABX pattern in spirocaracolitone G resonated at $\delta = 5.01$ with $J = 4.5$ and 1.5 Hz. This is consistent with this equatorial hydrogen coupling to the neighboring CH_2 group at $\delta = 2.01$ (dd, $J = 14.5$, 4.5 Hz) and at $\delta = 1.86$. The coupling constants in the latter peak could not be established since it overlapped with one of the acetyl methyl groups. The same pattern for H-21 and H-22 in spirocaracolitone H was found at $\delta = 5.38$, 1.88, and 1.93 as multiplets. This is summarized in Figure 2. Spirocaracolitone derivative B,[2] described earlier, showed these resonances at $\delta = 4.89$, 2.06, and 1.78. These structures were further confirmed by using 2D correlations (COSY, HMQC, and HMBC); see Table 1.

Spirocaracolitone I showed an additional acetoxy group when compared to derivative A. This substituent was eventually placed at C-11 on the basis of the following data. Spirocaracolitone E, for which we had an X-ray structure, carries an acetoxy group at C-11 and showed the remaining hydrogen at C-11 as a doublet at $\delta =$

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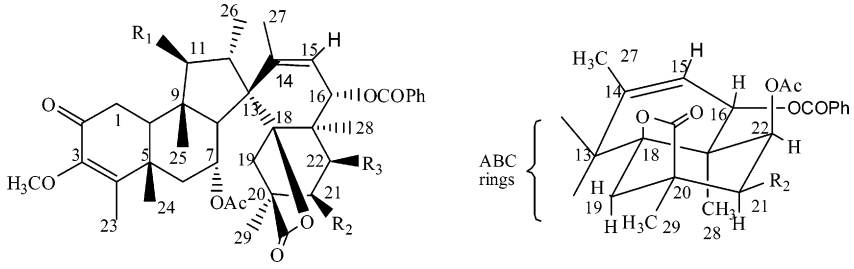
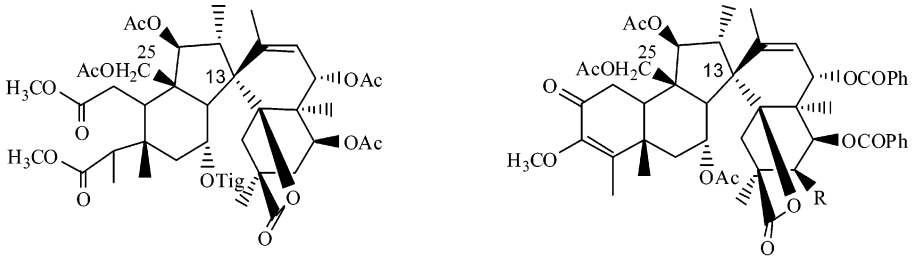


Chemical Shifts and Coupling patterns:

	H21	$H22_{eq}$
Spiro A	δ 5.20 or 5.23	δ 5.20 or 5.23
Spiro B	δ 2.06 (m), 1.78 (d, J = 14.4 Hz)	δ 4.89 (dd, J = 13.4, 4.0 Hz)
Spiro G	δ 1.86 (m), 2.01(dd, J = 4.5, 14.5 Hz)	δ 5.01 (dd, J = 14.5, 4.5 Hz)
Spiro H	δ 1.88 (m), 1.93 (m)	δ 5.38 (m)
Spiro I	δ 5.18 or 5.23 (d, J = 4.5 Hz)	δ 5.18 or 5.23 (d, J = 4.5 Hz)

Spirocaracolitone A: R_1 = H; R_2 = R_3 = OAc
Spirocaracolitone G: R_1 = R_2 = H; R_3 = OAc
Spirocaracolitone H: R_1 = R_2 = H; R_3 = OCOPh
Spirocaracolitone I: R_1 = R_2 = R_3 = OAc

Figure 2.

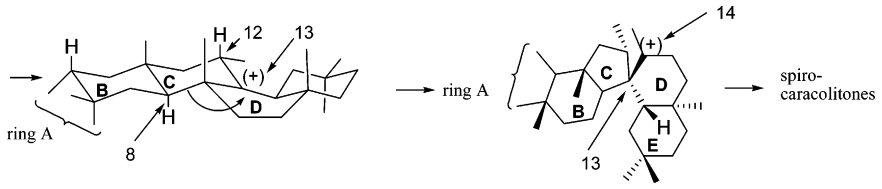


Spirocaracolitone E

Spirocaracolitone J: R = OAc
Spirocaracolitone K: R = H

Figure 3.

Scheme 1. Possible Biogenetic Route to the Spiro CD Ring System



5.22 (J = 13.0 Hz). A similarly spaced doublet (J = 12.0 Hz) is evident in the ^{1}H NMR spectrum of spirocaracolitone I at δ = 5.23. This proton is part of the spin system involving H-11, H-12, and the C-26 methyl group. The large coupling constant is consistent with the *trans* arrangement of H-11 and H-12. The C-11 and C-12 resonances in spirocaracolitones E and I occurred at δ = 82.2 and 44.4 and δ = 82.7 and 43.6, respectively. The 2D correlations (COSY, HMQC, and HMBC) are shown in Table 1.

The new spirocaracolitione derivatives J and K are further oxygenated and acetylated at the C-25 methyl group, respectively, relative to spirocaracolitoine I. Both compounds showed the expected AB quartet due to the C-25 diastereotopic hydrogens at δ = 5.14 (d, J = 13.0 Hz) and 4.49 (d, J = 13.0 Hz) for spirocaracolitone J and δ = 5.13 and 4.50 (d, J = 13.0 Hz) for spirocaracolitione K. The C-25 resonances were found at δ = 64.7 and 64.8 for spirocaracolitione J and spirocaracolitione K, respectively. The oxidation pattern of these compounds is reminiscent of those found in the spirocaracolitone derivative E, but without the ring A oxidatively cleaved structure of spirocaracolitone E.[2]

Spirocaracolitone K shows the same ABX pattern for the C-22 and C-21 hydrogens (δ = 1.96 (m), 2.31 (m), and 5.35 (dd, J = 4.5, 1.5 Hz)) as observed for the spirocaracolitone derivatives B, G, and H; spirocaracolitone K therefore lacks the C-21 acetoxy group. The carbon resonances at δ = 39.7 and 72.5 for C-21 and C-22, respectively, support this assignment. In contrast, spirocaracolitone J shows proton resonances at δ = 5.52 (d, J = 4.5 Hz) and 5.26 (d, J = 4.5 Hz) for H-21 and H-22 and at δ = 72.3 and 72.7 for C-21 and C-22, respectively. These structures have also been confirmed by 2D NMR techniques (COSY, HMQC, and HMBC; Table 2).

Finally, spirocaracolitone L (Figure 4) is the least oxidized of all the spirocaracolitones identified thus far. In particular, ring A of this compound is typical of friedelin itself, except for the introduction of the 1,2-double bond (H-2: δ = 6.07, dd, J = 3.0, 10.0 Hz; H-1: 6.77 dd, J = 1.5, 10.0 Hz). The resonances for C-1

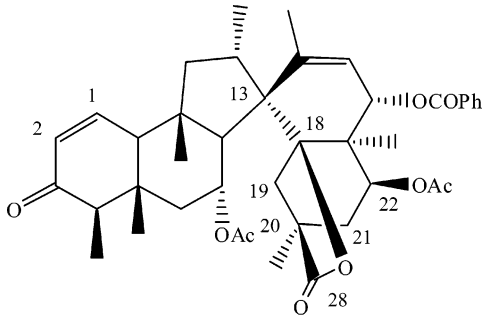


Figure 4.

Table 1. NMR Spectral Data of Spirocaracolitones G−I in $CDCl_3$

	compound G				compound H				compound I			
C/H no.	δC	δH (*J* in Hz)	COSY	HMBC	δC	δ (*J* in Hz)	COSY	HMBC	δC	δ (*J* in Hz)	COSY	HMBC
1_{ax}	37.1	2.35 m	10	2, 3, 10	37.2	2.35 m	10	2, 3, 10	36.3	2.21 m	10	2, 3, 10, 5
1_{eq}		2.59 dd (4.5, 17)		2, 3, 10, 5		2.60 dd (4.5, 17)		2, 3, 10, 5		2.51 m		2, 3, 10
2	193.9				194.0				192.6			
3	147.6				147.6				147.6			
4	155.2				155.3				153.9			
5	44.2				44.2				44.1			
6_{ax}	45.8	1.50 m	7	5, 7, 8, 24	45.9	1.51 m	7	5, 7, 8, 24	45.7	1.52 m	7	5, 7, 8, 24
6_{eq}		2.11 dd (3.0, 12.0)				2.15 m				2.11 dd (3.5,12.5)		
7	66.8	5.32 dt (3.5, 11.0)	6, 8	6, 8, C═O	66.9	5.32 dt (3.5, 10.5)	6, 8	6, 8, C═O	66.0	5.40 m	6, 8	5,6, 8, C═O
8	61.6	2.44 d (12.5)	7	7, 9, 13, 25	61.5	2.40 m	7	7, 9, 13, 25	55.0	2.34 d (11.5)	7	6, 7, 9, 13
9	41.8				41.85				41.6			
10	55.8	1.85 m	1	1, 2, 5, 9	55.8	1.85 m	1	1, 2, 5, 9	56.1	1.91 m	1	1, 2, 5, 9
11	50.3	1.50 m	12	9, 12	50.5	1.50 m	12	9, 12	82.7	5.23 d (12.0)	12	9, 12,C═O
12	40.4	2.91 m	11, 26	11, 13, 26	39.9	2.97 m	11, 26	11, 13, 26	43.8	2.95 m	11, 26	11, 13, 26
13	57.5				57.6				54.6			
14	136.4				136.1				135.4			
15	125.7	5.47 brs	16, 27	14, 16, 17, 27	125.8	5.49 brs	16, 27	14, 16, 17, 27	126.5	5.39 brs	16	14, 16, 17, 27
16	70.4	6.01 brs	15	15, 17, C═O	70.8	5.96 m	15	15, 17, C═O	69.0	5.77 brs	15	15, 17, C═O
17	44.6				44.9				45.6			
18	91.2				91.3				89.8			
19_{ax}	42.1	2.35 m		18, 20	42.3	2.51 d (12.5)		18, 20	43.4	2.47 m		18, 20
19_{eq}		1.50 m				2.35 m				2.70 m		
20	39.3				44.9				46.8			
21_{ax}	37.2	2.01dd (4.5, 14.5)	22	20, 22	39.7	1.93 m	22	20, 22	72.0	5.18 d (4.5)	22	20, 22, C═O
21_{eq}		1.86 m				1.88 m						
22	72.7	5.01 dd (1.5, 4.5)	21	21, 17, C═O	72.9	5.38 m	21	21, 17, C═O	72.6	5.15 d (4.5)	21	21, 17, C═O
23	11.3	1.86 s			11.3	1.86 s			11.2	1.82 s		
24	18.5	1.24 s			18.6	1.22 s			18.1	1.29 s		
25	19.4	1.32 s			19.4	1.24 s			20.3	1.32 s		
26	17.8	1.18 d (7.5)	12		17.8	1.19 d (7.5)	12		13.8	1.01 d (7.5)	12	
27	24.0	1.84 s	15		23.9	1.84 s	15		23.8	1.91 s		
28	20.8	1.39 s	16		21.0	1.48 s	16		16.4	1.39 s		
29	20.6	1.29 s			20.4	1.29 s			20.8	1.29 s		
30	178.4				178.4				175.7			
OCH_3	59.6	3.58 s		3	59.6	3.61 s		3	59.6	3.58 s	3	3
Acetyl:												
MeCOO	21.32	1.87 s			21.2	1.89 s			20.4	1.95 s		
MeCOO	21.39	2.3 s							21.1	1.97 s		
MeCOO									21.9	2.01 s		
MeCOO									22.6	2.20 s		
MeCOO	169.6				171.7				169.9			
MeCOO	171.6								170.2			
MeCOO									170.6			
MeCOO									171.5			
Benzoyl:												
1′	129.9				130.0				129.2			
2′, 6′	129.3	7.93 m	3′, 5′		129.6	7.82 m	3′, 5′		129.7	7.98 m	3′, 5′	
3′, 5′	128.4	7.41 m	2′, 6′, 4′		128.1	7.34 m	2′, 6′, 4′		128.6	7.59 m	2′, 6′	
4′	133.1	7.52 m	3′, 5′		133.0	7.48 m	3′, 5′		133.7	7.45 m	3′, 5′	
C═O	165.9				165.5				165.9			
Benzoyl:												
1″					129.4	7.82 m	3′, 5′					
2″, 6″					129.2	7.34 m	2′, 6′, 4′					
3″, 5″					128.1	7.48 m	3′, 5′					
4″					132.8							
C═O					164.8							

and C-2 occurred at $\delta = 147.9$ and 130.6, respectively.[7] The H-21−H-22 spin system $\delta = 1.96$ (m, $H21_{ax}$), 2.10 (m, $H21_{eq}$), 5.35 (dd, $J = 1.5$, 4.5, H22) was readily identified since it is reminiscent of that found in the spirocaracolitone derivatives A, D, G, and H. For the 2D assignments see COSY, HMQC, and HMBC in Table 2.

It seems plausible that this compound is the precursor of all the others via further oxygenation and acylation at various sites. The nature of ring A in spirocaracolitone derivative L indicates that the rearrangement from the typical pentacyclic triterpene to the ring C and D spiro structures in these compounds as proposed earlier[2] occurs prior to the generation of the 2-keto-3-methoxy-3-ene functionality in ring A. The ring A structure in spirocaracolitone L, although relatively rare in triterpenoids, is present in compounds isolated from the root bark of *Salacia prenoides*.[8] A relatively straightforward pathway for the conversion of the ring A structure of spirocaracolitone L to that of the other spiro derivatives is proposed in Scheme 2. This involves the epoxidation of (1) a double bond to give (2) the opening of the expoxide with concomitant migration of H-2 to give the 2,3-dione (3), enolization toward C-4, and finally, O-methylation (4).

Scheme 2. Proposed Mechanism for the Conversion of Ring A in Spirocaracolitone I to the Ring A Pattern in the Other Derivatives

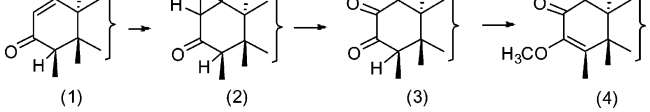


Table 2. NMR Spectral Data of Spirocaracolitones J−L in $CDCl_3$

	compound J				compound K				compound L			
C/H no.	δC	δ (*J* in Hz)	COSY	HMBC	δC	δ (*J* in Hz)	COSY	HMBC	δC	δ.(*J* in Hz)	COSY	HMBC
1_{ax}	39.2	2.47 m	10	2, 3, 10	39.2	2.50 dd (3.5, 18)	10	2, 3, 10	130.6	6.07 dd (3.0, 10.0)	2, 10	2, 3, 10, 5
1_{eq}		3.08 m	10	2, 10		3.08 m		2, 10				
2	193.2				193.3				147.9	6.77 dd (1.5, 10.0)	1	1, 3, 10
3	147.6				147.6				200.7			
4	153.7				153.8				57.9	2.33 q (6.5)	23	2, 3, 5, 23
5	44.1				41.8				44.6			
6_{ax}	46.1	1.50 m	7	5, 7, 8, 24	46.1	1.50 m	7	5, 7, 8, 24	47.6	1.50 m	7	5, 7, 8, 24
6_{eq}		2.25 dd (3.5, 12.5)				2.25 m				2.02 dd (3.5,12.5)		
7	65.1	5.46 m	6, 8	6, 8, C═O	65.2	5.45 m	6, 8	6, 8, C═O	66.9	5.25 m	6, 8	5,6, 8, C═O
8	56.3	2.56 d (11.5)	7	7, 9, 13	56.4	2.58 d (12.0)	7	7, 9, 13	62.6	2.42 d (11.5)	7	6, 7, 9, 13
9	41.8				44.7				40.6			
10	55.9	2.20 m	1	1, 2, 5, 9	55.9	2.25 m	1	1, 2, 5, 9	61.0	2.39 m	1	1, 2, 5, 9
11_{ax}	82.1	5.42 m	12	9, 12, C═O	82.2	5.43 m	12	9, 12, C═O	50.4	1.52 m	12	9, 12
11_{eq}										1.71 dd (5.5, 12.0)		
12	44.0	3.08 m	11, 26	11, 13, 26	45.0	3.08 m	11, 26	11, 13, 26	39.6	2.96 m	11, 26	11, 13, 26
13	54.5				54.6				57.3			
14	134.5				134.3				136.0			
15	127.4	5.45 brs	16, 27	14, 16, 27	127.7	5.45 brs	16, 27	14, 16, 27	125.9	5.37 brs	16, 27	14, 16, 17, 27
16	69.3	5.46 m	15	15, 17, C═O	69.9	5.68 m	15, 28	15, 17, C═O	70.2	5.70 m	15	15, 17, C═O
17	47.6				47.7				45.2			
18	89.6				90.4				91.2			
19_{ax}	43.5	2.47 m		18, 20	39.7	1.96 m		18, 20	42.4	2.39 m		18, 20
19_{eq}		2.77 m				2.09 m				2.50 d (12.5)		
20	47.0				40.8				44.0			
21_{ax}	72.3	5.52 d (4.5)	22	20, 22, C═O	43.4	2.35 dd (2.0, 12.5)	22	20, 22	39.8	1.96 m	22	20, 22
21_{eq}						2.58 d (12.0) m				2.31 m		
22	72.7	5.26 d (4.5)	21	21, 17, C═O	72.5	5.34 d (3.0)	21	21, 17, C═O	72.6	5.35 dd (1.5, 4.5)	21	21, 17, C═O
23	11.5	1.89 s			11.5	1.89 s			7.3	1.02 d (6.5)	4	
24	18.3	1.28 s			18.3	1.23 s			16.0	0.94 s		
25_{ax}	64.7	5.14 d (13.0)	25_{eq}		64.8	4.50 d (13.0)	25_{eq}		18.3	1.26 s		
25_{eq}		4.49 d (13.0)	25_{ax}			5.13 d (13.0)	25_{ax}					
26	13.7	1.08 d (7.5)	12		13.7	1.08 d (7.5)	12		17.9	1.12 d (7.5)	12	
27	23.5	1.90 s	15		23.6	1.89 s	15		23.7	1.84 s		
28	16.2	1.33 s			20.5	1.28 s	16		20.7	1.32 s		
29	20.9	1.40 s			20.9	1.34 s			20.6	1.29 s		
30	175.5				177.9				178.4			
OCH_3	59.6	3.61 s		3	59.7	3.61 s		3				
Acetyl:												
MeCOO	20.2	1.82 s			20.3	1.82 s			21.8	1.84 s		
MeCOO	20.4	1.85 s			20.5	1.84 s			21.0	2.09 s		
MeCOO	20.4	1.89 s			20.8	2.12 s						
MeCOO	20.8	2.08 s										
MeCOO	170.0				170.1				170.1			
MeCOO	170.0				170.2				171.6			
MeCOO	170.2				171.4							
MeCOO	171.3											
Benzoyl:												
1′	128.9				129.2				129.3			
2′, 6′	129.8	8.0 m	3′, 5′		129.7	8.0 m	3′, 5′		129.7	8.0 m	3′, 5′	
3′, 5′	128.6	7.58 m	2′, 6′, 4′		128.6	7.58 m	2′, 6′, 4′		128.3	7.39 m	2′, 6′	
4′	133.8	7.44 m	3′, 5′		133.8	7.46 m	3′, 5′		133.3	7.54 m	3′, 5′	
C═O	165.7				165.7				165.1			
Benzoyl:												
1″	128.7				129.0							
2″, 6″	129.7	8.0 m	3′, 5′		129.7	8.0 m	3′, 5′					
3″, 5″	128.4	7.58 m	2′, 6′, 4′		128.3	7.58 m	2′, 6′, 4′					
4″	133.5	7.44 m	3′, 5′		133.4	7.46 m	3′, 5′					
C═O	165.5				165.0							

Conclusion

The profile of compounds observed in this collection from the eastern side of Osa suggests the possibility of subspecies or varieties with slightly different chemical defense systems. Alternatively, environmental factors, such as attack by insect or fungal pests or time of collection (wet/dry season), or differences in the age of the trees may be the cause of the distinct phytochemical profiles observed. Several new collections are being initiated to address these issues. Investigations of the constituents of other parts of *R. caracolito* are currently under way and may provide support for the proposed biosynthetic pathway from the pentacyclic friedelin structure to the CD spirocaracolitione structures found in these compounds.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Melting points were determined by using a Thomas-Hoover Capillary melting point apparatus. ESIMS data were obtained using a Micromass Quattro LC instrument. IR spectra were recorded on a Shimadzu 8400-S FT/IR spectrometer. NMR spectra were obtained in $CDCl_3$ on a Bruker AMX-500 NMR spectrometer. Solvents for extractions and chromatographic purifications were routinely distilled before use. Column chromatographic purifications were performed with silica gel 270−400 mesh. Preparative HPLC work was performed on a LC-908 JAIGEL recycling HPLC equipped with a fixed-wavelength UV detector (254 nm) and a 15 mm reversed-phase column (ODS-S-343-15). HPLC-grade aceto-

nitrile (Omnisolv) was filtered through Millipore filters before use. Water for HPLC work was obtained from a Millipore filtration system.

Collection, Extraction, and Isolation Procedures. The bark of *R. caracolito* was collected in Golfito, Costa Rica, and preserved in 1 L Nalgene bottles containing 95% EtOH for transport into Canada. A voucher specimen has been deposited in the herbarium of the Univeristy of Ottawa (No. 19109). The EtOH was eventually decanted and put aside, while the bark was allowed to dry in the fumehood overnight. When the bark was dry, it was ground into sawdust-sized particles using a Wiley mill. The ground bark was soaked in CH_2Cl_2 and extracted three times at room temperature for a 2-day period. The combined extracts were evaporated using a rotary evaporator, yielding a gummy, brownish solid.

The CH_2Cl_2-soluble extract was then subjected to flash chromatography eluted with CH_2Cl_2/acetone in a gradient of 0 to 100% and resulted in the collection of different fractions containing the spirocaracolitones. The different fractions collected from crude chromatography were further subjected to flash chromatography eluted with CH_2Cl_2/acetone and resulted in the partial subdivision of these compounds. The final separation of these six new spirocaracolitones was done using a recycling HPLC equipped with a preparative reversed-phase column eluted at a rate of 4 mL·min^{-1}, with either 30% H_2O in MeCN or 30% H_2O in MeOH.

Spirocaracolitone G: yield 0.002%; mp 212−214.°C; $[\alpha]^{25}_D$ −19.5 (*c* 0.005, CH_2Cl_2); IR 1785, 1747, 1724, 1674 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.35 (1 H, m, $H1_{ax}$), 2.59 (1 H, dd, J = 14.5, 17.0 Hz, $H1_{eq}$), 1.50 (1 H, m, $H6_{ax}$), 2.11 (1 H, dd, J = 3.0, 12.0 Hz, $H6_{eq}$), 5.32 (1 H, dt, J = 3.5, 11.0 Hz, H7), 2.44 (1 H, d, J = 12.5 Hz, H8), 1.85 (1 H, m, H10), 1.35−1.50 (2 H, m, H11), 2.91 (1 H, m, H12), 5.47 (1 H, m, H15), 6.01 (1 H, m, H16), 2.35 (1 H, m, $H19_{eq}$), 1.50 (1 H, m, $H19_{ax}$), 2.01 (1 H, dd, J = 4.5, 14.5 Hz, $H21_{eq}$), 1.86 (1 H, m, $H21_{ax}$), 5.01 (1 H, dd, J = 1.5, 4.5 Hz, H22), 1.86 (3 H, s, H23), 1.22, 1.22, 1.39 (3 s, H24, H25, and/or H28), 1.18 (3 H, d, J = 7.5 Hz, H26), 1.84 (3 H, brs, H27), 1.29 (3 H, s, H29), 3.63 (3 H, s, OMe), 1.87, 2.30 (2 s, 2 × MeCO), benzoyl group: 7.93 (2 H, m, H2′), 7.52 (1 H, m, H4′), 7.41 (2 H, m, H3′); ESIMS *m*/*z* 733 $[M + NH_4]^+$ (67), 717 $[MH]^+$ (100); HRESIMS *m*/*z* 717.35940 $[MH]^+$ (calcd for $C_{42}H_{52}O_{10}$, 717.35621).

Spirocaracolitone H: yield 0.0024%; mp 226−228 °C; $[\alpha]^{25}_D$ −25.2 (*c* 0.004, CH_2Cl_2); IR 1780, 1748, 1725, 1674 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.35 (1 H, m, $H1_{ax}$), 2.60 (1 H, dd, J = 14.5, 17.0 Hz, $H1_{eq}$), 1.51 (1 H, m, $H6_{ax}$), 2.15 (1 H, m, $H6_{eq}$), 5.32 (1 H, dt, J = 3.5, 10.5 Hz, H7), 2.40 (1 H, m, H8), 1.85 (1 H, m, H10), 1.30−1.50 (2 H, m, H11), 2.97 (1 H, m, H12), 5.49 (1 H, brs, H15), 5.96 (1 H, brs, H16), 2.35 (1 H, m, $H19_{ax}$), 2.51 (1 H, d, J = 12.5 Hz, $H19_{eq}$), 1.88 (1 H, m, $H21_{ax}$), 1.93 (1 H, m, $H21_{eq}$), 5.38 (1 H, m, H22), 1.86 (3 H, s, H23), 1.22, 1.22, 1.48 (3 s, H24, H25, and/or H28), 1.20 (3 H, d, J = 7.5 Hz, H26), 1.84 (3 H, s, H27), 1.29 (s3 H, H29), 3.61 (3 H, s, OMe), 2.23 (s, MeCO), benzoyl groups: 7.82 (4 H, m, H2′/ H2″), 7.48 (2 H, m, H4′/H4″), 7.34 (4 H, m, H3′/H3′); ESIMS *m*/*z* 795 $[M + NH_4]^+$ (41.4), 779 $[MH]^+$ (100); HRESIMS *m*/*z* 779.37505 $[MH]^+$ (calcd for $C_{47}H_{54}O_{10}$, 779.37327).

Spirocaracolitone I: yield 0.0018%; mp 210−212 °C; $[\alpha]^{25}_D$ −11.6 (*c* 0.005, CH_2Cl_2); IR 1779, 1750, 1720, 1678 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.21 (1 H, m, $H1_{ax}$), 2.51 (1 H, m, $H1_{eq}$), 1.52 (1 H, m, $H6_{ax}$), 2.11 (1 H, dd, J = 3.5, 12.5 Hz, $H6_{eq}$), 5.40 (1 H, m, H7), 2.34 (1 H, d, J = 11.5 Hz, H8), 1.91 (1 H, m, H10), 5.23 (d, J = 1 H, 12.0 Hz, H11), 2.95 (1 H, m, H12), 5.39 (1 H, brs, H15), 5.77 (1 H, brs, H16), 2.47 (1 H,m, $H19_{ax}$), 2.70 (1 H, m, $H19_{eq}$), 5.18 (1 H, d, J = 4.5 Hz, H21), 5.15 (1 H, d, J = 4.5 Hz, H22), 1.82 (3 H, s, H23), 1.29, 1.32, 1.39 (3 s, H24, H25, and/or H28), 1.01 (3 H, d, J = 7.5 Hz, H26), 1.91 (3 H, brs, H27), 1.29 (3 H, s, H29), 3.58 (3 H, s, OMe), 1.97, 1.95, 2.01, 2.20 (4 × s, 4 × MeCO), benzoyl group: 7.98 (2H, m, H2′), 7.59 (1 H, m, H4′), 7.45 (2 H, m, H3′); ESIMS *m*/*z* 871 [M + K]$^+$ (77.62), 833 $[MH]^+$ (1.82); HRESIMS *m*/*z* 833.37036 $[MH]^+$ (calcd for $C_{46}H_{56}O_{14}$, 833.37385).

Spirocaracolitone J: yield 0.0022%; mp 240 °C dec; $[\alpha]^{25}_D$ −15.2 (*c* 0.005, CH_2Cl_2); IR 1780, 1750, 1720, 1675 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.47 (1 H, m, $H1_{ax}$), 3.08 (1 H, m, $H1_{eq}$), 1.50 (1 H, m, $H6_{ax}$), 2.25 (1 H, dd, J = 3.5, 12.5 Hz, $H6_{eq}$), 5.46 (1 H, m, H7), 2.56 (1 H, d, J = 11.5 Hz, H8), 2.20 (1 H, m, H10), 5.42 (1 H, m, H11), 3.08 (1 H, m, H12), 5.45 (1 H, brs, H15), 5.77 (1 H, brs, H16), 2.47 (1 H, m, $H19_{ax}$), 2.77 (1 H, d, J = 13.0 Hz, $H19_{eq}$), 5.52 (1 H, d, J = 4.5 Hz, H21), 5.26 (1 H, d, J = 4.5 Hz, H22), 1.89 (3 H, s, H23), 1.28, 1.33 (2 s, H24, and/or H28), 5.14 (1 H, d, J = 13.0 Hz, $H25_{eq}$), 4.49 (1 H, d, J = 13.0 Hz, $H25_{ax}$), 1.08 (3 H, d, J = 7.5 Hz, H26), 1.90 (3 H, s, H27), 1.40 (3 H, s, H29), 3.61 (3 H, s, OMe), 1.85, 1.82, 1.89, 2.08 (4 × s, 4 × MeCO), benzoyl groups: 8.0 (4 H, m, H2′/ H2″), 7.58 (2 H, m, H4′/H4″), 7.44 (4 H, m, H3′/H3″); ESIMS *m*/*z* 971 $[M + NH_4]^+$ (8.52), 953 $[MH]^+$ (100); HRESIMS *m*/*z* 953.39149 $[MH]^+$ (calcd for $C_{53}H_{60}O_{16}$, 953.39081).

Spirocaracolitone K: yield 0.002%; mp 230 °C dec; $[\alpha]^{25}_D$ −24.5 (*c* 0.006, CH_2Cl_2); IR 1781, 1748, 1722, 1675 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.08 (1 H, m, $H1_{ax}$), 2.50 (1 H, dd, J = 3.5, 18.0 Hz, $H1_{eq}$), 1.50 (1 H, m, $H6_{ax}$), 2.25 (1 H, m, $H6_{eq}$), 5.45 (1 H, m, H7), 2.58 (1 H, d, J = 12.0 Hz, H8), 2.25 (1 H, m, H10), 5.43 (1 H, m, H11), 3.08 (1 H, m, H12), 5.45 (1 H, brs, H15), 5.68 (1 H, m, H16), 2.09 (1 H, m, $H19_{ax}$), 1.96 (1 H, m, $H19_{eq}$), 2.35 (1 H, dd, J = 3.0, 12.5 Hz, $H21_{ax}$), 2.58 (1 H, d, J = 12.0 Hz, $H21_{eq}$), 5.34 (1 H, d, J = 3.0 Hz, H22), 1.89 (3 H, s, H23), 1.23, 1.28 (H24, 2 s, and/or H28), 5.13 (1 H, d, J = 13.0 Hz, $H25_{eq}$), 4.50 (1 H, d, J = 13.0 Hz, $H25_{ax}$), 1.08 (3 H, d, J = 7.5 Hz, H26), 1.89 (3 H, s, H27), 1.34 (3 H, s, H29), 3.61 (3 H, s, OMe), 1.82, 1.84, 2.12 (3 × s, 3 × MeCO), benzoyl groups: 8.0 (4 H, m, H2′/H2″), 7.58 (2 H, m, H4′/H4″), 7.46 (4 H, m, H3′/H3″); ESIMS *m*/*z* 913 $[M + NH_4]^+$ (14.18), 895 $[MH]^+$ (100); HRESIMS *m*/*z* 895.38601 $[MH]^+$ (calcd for $C_{51}H_{58}O_{14}$, 895.38206).

Spirocaracolitone L: yield 0.0028%; mp 194−197 °C; $[\alpha]^{25}_D$ −20.5 (*c* 0.005, CH_2Cl_2); IR 1775, 1752, 1720, 1674 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.07 (1 H, dd, J = 3.0, 10.0 Hz, H1), 6.77 (1 H, dd, J = 1.5, 10.0 Hz, H2), 2.33 (1 H, q, J = 6.5 Hz, H4), 1.50 (1 H, m, $H6_{ax}$), 2.02 (1 H, dd, J = 3.5, 12.5 Hz, $H6_{eq}$), 5.25 (1 H, dt, J = 3.5, 11.5 Hz, H7), 2.42 (1 H, d, J = 11.5 Hz, H8), 2.39 (1 H, m, H10), 1.52 (1 H, m, $H11_{ax}$), 1.71 (1 H, dd, J = 5.5, 12.0 Hz, $H11_{eq}$), 2.96 (1 H, m, H12), 5.37 (1 H, m, H15), 5.70 (1 H, m, H16), 2.39 (1 H, m, $H19_{ax}$), 2.50 (1 H, d, J = 12.5 Hz, $H19_{eq}$), 1.96 (1 H, m, $H21_{ax}$), 2.31 (1 H, m, $H21_{eq}$), 5.35 (1H, dd, J = 1.5, 4.5 Hz, H22), 1.02 (3 H, d, J = 6.5 Hz, H23), 0.94, 1.26, 1.32 (3 s, H24, H25, and/or H28), 1.12 (3 H, d, J = 7.5 Hz, H26), 1.84 (3 H, brs, H27), 1.25 (3 H, s, H29), 1.84, 2.09, (2 × s, 2 × MeCO), benzoyl group: 8.0 (2 H, m, H2′), 7.50 (1 H, m, H4′), 7.39 (2 H, m, H3′); ESIMS *m*/*z* 703 $[M + NH_4]^+$ (100), 687 $[MH]^+$ (0.68); HRESIMS *m*/*z* 687.34884 $[MH]^+$ (calcd for $C_{41}H_{50}O_9$, 687.34591).

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of all compounds named as spirocaracolitones G−L. This material is available free of charge via the Internet at http://pubs.acs.org.

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