New Pyranocoumarins Isolated from *Calophyllum lanigerum* and *Calophyllum teysmannii*[1]

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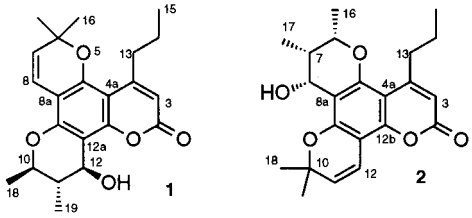
During a chemotaxonomic survey of *Calophyllum* extracts present in the National Cancer Institute's natural product repository, four new pyranocoumarins were isolated from extracts of *C. lanigerum* var. *austrocoriaceum* and *C. teysmannii* var. *inophylloide* (King.) P. F. Stevens (Clusiaceae). The structure elucidation and anti-HIV activity of calanolide E2 (**4**), cordatolide E (**5**), pseudocordatolide C (**6**), and calanolide F (**9**), along with a simple prenylated coumarin precursor (**11**), are described here.

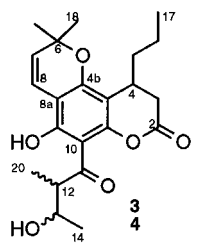
As part of our ongoing effort to isolate and identify novel anti-HIV agents from a variety of natural sources, our laboratory reported the discovery of a family of HIV-inhibitory pyranocoumarins, the calanolides, from the tropical tree *Calophyllum lanigerum* Miq. var. *austrocoriaceum* (T. C. Whitmore) P. F. Stevens (Clusiaceae).[2] (+)-Calanolide A (**1**), the lead compound of this series, first defined this unique new subclass of non-nucleoside HIV-1 reverse transcriptase inhibitor.[3]

Pyranocoumarins isolated from *Calophyllum* fall into one of three basic structural types: (a) tetracyclic dipyranocoumarins, in which the C rings have a *gem*-dimethyl group, for example, calanolide A (**1**); (b) tetracyclic dipyranocoumarins with reversed C and D pyran rings, that is, the *gem*-dimethyl groups are found in the D ring, as in pseudocalanolide C (**2**);[4] and (c) tricyclic pyranocoumarins, for example, calanolide E1 (**3**),[2] which contain a noncyclized equivalent of the D ring of the calanolide structure class. Individual members of the groups vary with respect to the C4 substituent on the lactone ring of the coumarin, where methyl, *n*-propyl, or phenyl groups may be encountered. As part of a chemotaxonomic survey of *Calophyllum* extracts present in the Nation Cancer Institute's (NCI) natural product repository,[5] four new pyranocoumarins, representing all three structure types, have been isolated from extracts of *C. lanigerum* Miq. var. *austrocoriaceum* (T. C. Whitmore) P. F. Stevens and *Calophyllum teysmannii* Miq. var. *inophylloide* (King.) P. F. Stevens (Clusiaceae). The structure elucidation and anti-HIV activity of these compounds are described here.

Results and Discussion

Four organic extracts of *C. lanigerum* were analyzed for pyranocoumarin content. Of the extracts investigated, one from stembark contained only tricyclic pyranocoumarins, while three from leaves contained both types of tetracyclic pyranocoumarins. The stembark extract from our original collection of *C. lanigerum* var. *austrocoriaceum* contained, as the major component, calanolide E1 (**3**), which was originally isolated with **1** from the original collection[2] and is the major component of the latex of *C. lanigerum* var. *austrocoriaceum*.[6] In addition to **3**, two new tricyclic pyranocoumarins were isolated. The first of these (**4**) had a molecular formula of $C_{22}H_{28}O_6$ based on HRFABMS, isomeric with calanolide E1 (**3**). Comparison of the ^{1}H-NMR spectra of the two compounds revealed their close structural similarity. Differences in the spectrum of **4** were principally in the C11−C14 portion of the molecule. For example, H-13 was shifted upfield from δ 4.49 in **3** to 4.10 in **4**, while both methyls in this portion of the molecule appeared downfield in **4** (Me-14, δ 1.35 to 1.45; Me-20, δ 1.12 to 1.29). In addition, the carbon resonances in the same part of the molecule were downfield relative to those of calanolide E1 (δ 45.7, 78.8, 19.5, and 10.5 vs. δ 44.2, 76.1, 16.2, and 9.3 for C12, C13, C14, and C20, respectively, in **4** vs. **3**). These changes in chemical shifts, coupled with the differences in the optical rotations for the two compounds ($[\alpha]_D$ +28.4° for **3**, +79.1° for **4**), indicated that they were diastereomers. Therefore, we refer to **4** as calanolide E2. The ^{1}H and ^{13}C resonances were assigned using a combination of COSY, HMQC, and HMBC experiments, along with comparisons to **3** (Tables 1 and 2).





The second new tricyclic pyranocoumarin (**5**) had a molecular formula of $C_{20}H_{24}O_6$, corresponding to a difference of C_2H_4 from calanolide E1 (**3**). This difference could easily be accounted for from the ^{1}H-NMR spectrum, which indicated that **5** contained a methyl substituent at C4, instead of an *n*-propyl group; this

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Table 1. ^{1}H-NMR Assignments for Compounds **4**, **5**, **6**, **9**, and **11**[a]

	4	**5**	**6**	**9**	**11**
H	δ, mult., *J* Hz	δ, mult., *J* Hz	δ, mult., *J* Hz	δ, mult., *J* Hz	δ, mult., *J* Hz
3	2.67, br dd, 8.8, 14.7 2.80, dd, 7.8, 14.7	2.81, dd, 8.0, 15.2 2.64, dd, 7.6, 15.2	5.92, s	5.95, t, 1.0	5.93, s
4	3.66, br m	3.75, ddd, 8.0, 7.6, 7.3			
6			4.33, dq, 2.5, 6.8		6.32, s
7	5.43, d, 9.8	5.44, d, 10.0	2.22, ddq, 2.5, 6.9, 6.2	5.54, d, 10.5	
8	6.59, d, 9.8	6.58, d, 10.0	5.02, d, 6.2	6.65, d, 10.5	
8b					
10				4.50, dq, 2.0, 6.8	
11			5.56, d, 10.0	2.03, m	6.37, dq, 1.0, 6.5
12	2.50, dq, 7.3, 8.8	4.51, dq, 3.4, 7.1	6.82, d, 10.0	4.86, d, 2.0	1.83, d, 6.5
13	4.10, dq, 5.2, 8.8	2.52, dq, 3.4, 7.1	2.5, s	2.88, m	2.84, t, 7.5
14	1.45, d, 5.2	1.34, d, 7.1	1.39, d, 6.8	1.65, sext, 7.7	1.60, sext, 7.5
15	1.50, m	1.24, d, 7.3	1.07, d, 6.9	1.03, t, 7.7	1.00, t, 7.5
16	1.80, m	1.42, s	1.51, s	1.49, s	3.94, s
17	0.84, t, 7.3	1.37, s	1.45, d	1.48, s	3.84, s
18	1.42, s	1.11, d, 7.1		1.43, d, 6.8	1.94, d, 1.0
19	1.42, s			0.79, d, 7.5	
20	1.29, d, 7.3				
OH	12.4, s				

[a] All spectra recorded in $CDCl_3$, internal reference δ 7.24 (residual $CHCl_3$).

Table 2. ^{13}C-NMR Assignments for **4**, **5**, **6**, **9**, and **11**[a]

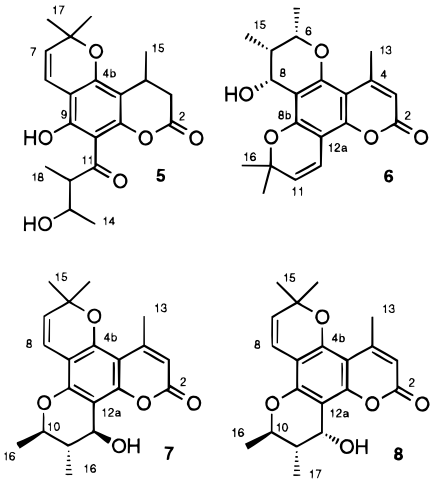
C no.	**4**	**5**	**6**	**9**	**11**
2	178.7	178.5	160.4	160.9	160.2
3	38.4	39.3	111.2	110.5	111.1
4	30.4	25.5	154.6	158.8	157.5
4a	108.8	110.6	104.0	103.3	103.9
4b	157.0	157.3	152.8	151.4	
5					159.2
6	78.1	78.2	75.2	71.1	91.0
7	125.7	125.7	34.8	126.8	159.0
8	115.7	115.6	64.6	116.5	111.3
8a	102.6	102.7	108.9	104.1	153.2
8b	159.9		154.6	153.3	
9		160			194.3
10	101.8	101.3	78.7	77.8	139.3
10a	159.9				
11	199.3	201.0	126.7	38.5	143.1
12	45.7	44.2	115.6	64.7	15.1
12a			113.8	106.2	
12b			150.2	155.0	
13	78.8	76.1	24.2	37.5	38.6
14	19.5	16.2	16.2	23.4	22.8
15	35.5	19.2	7.3	14.0	14.1
16	20.7	28.1	28.2	27.4	56.1
17	14.0	28.4	27.7	28.0	56.0
18	28.0	9.3		18.9	10.7
19	28.4			15.1	
20	10.5				

[a] All spectra recorded in $CDCl_3$ with internal referencing to δ 77.0.

assignment was based on the absence of the triplet methyl signal at δ 0.84 and the two methylene signals at δ 1.80 and 1.50 as well as the presence of a doublet methyl signal at δ 1.24. These differences were accompanied by the appearance of the H4 resonance downfield at δ 3.75 and the *gem*-dimethyl signals slightly upfield (δ 1.45 and 1.41 in **3**, compared to δ 1.42 and 1.37 in **5**). The ^{13}C-NMR spectrum showed analogous features. The *n*-propyl carbon signals in **3** occurred at δ 35.4, 20.7, 14.0, whereas the single methyl signal of **5** appeared at δ 19.2; small differences in the carbon chemical shifts (< 2 ppm) of the neighboring carbons (C3 and C4a) were accompanied by a 5-ppm upfield appearance of C4 to δ 30.5. Complete assignments of the proton and carbon signals for cordatolide E (**5**) are provided in Tables 1 and 2.

Extracts of three different leaf collections of *C. lanigerum* var. *austrocoriaceum* were chemically distinct from the bark extract described above. These extracts contained a new member of the pseudocalanolide series. HREIMS established a molecular formula of $C_{20}H_{22}O_5$. The compound was identified as a member of the pseudocalanolide class, based on the characteristic H12 resonance at δ 6.82,[4] which is 0.2 ppm downfield of the corresponding H8 signal for the calanolide series (e.g., δ 6.60 for H8 of calanolide A[2]). This new compound also had a methyl substituent at C4 (singlet methyl signal at δ 2.5). The major structural challenge of the pyranocoumarins is the assignment of the carbon resonances of the completely substituted phenyl ring of the coumarin core, due to the close chemical shifts of the three carbons bearing oxygen substituents (i.e., C4b, C8b, and C12b). However, the assignment of the carbons is generally possible with HMBC experiments optimized for long-range C−H coupling constants of 8.3 and 5.5 Hz. Correlations from the carbon signal at 104.0 ppm to the singlet at δ 2.5 (Me-13) and H3 (δ 5.9) placed this carbon at C4a. Correlations to H6 and H8 (δ 4.32 and 5.01 ppm, respectively) from carbons at δ 152.8 and 108.9 suggested these signals were C4b and C8a, respectively. Correlations were also observed to H8 (δ 5.01) and H12 (δ 6.82) from a carbon at δ 154.6, identifying it as C8b. Finally, correlations to H12 (δ 6.82) from carbon signals at δ 113.8 and 150.2 led to their assignment as C12a and C12b, respectively. In a similar manner, the remaining correlations provided the gross structure of **6** as shown (see Tables 1 and 2). A literature survey indicated that **6** was the first pseudoanalogue of the cordatolides, reported from *C. cordatooblongum*.[7] Comparison of the coupling constants of **6** with those of the known cordatolides A (**7**) and B (**8**)[7] indicated that their coupling constants did not match those for **6**. However, comparison of **6** with pseudocalanolide C (**2**) showed a close match of both chemical shifts and coupling constants for H6, H7, and H8. These closely matched coupling constants for **2** and **6**, suggesting that they had the same relative stereochemistry; consequently, we have named the compound pseudocordatolide C (**6**). In addition, because pseudocalanolide C and pseudocordatolide C differ only in their C4

substituents, because they both have similar optical rotations ($[\alpha]_D$ +68° for **2**, +67° for **6**), and because the absolute stereochemistry of **2** has been determined, pseudocordatolide C must have the same absolute stereochemistry [6*S*, 7*S*, 8*R*]. Unfortunately, this could not be experimentally confirmed due to paucity of the natural product.



Examination of an organic extract of leaves and twigs of *C. teysmannii* var. *inophylloide* led to a new pyranocoumarin (**9**) of the calanolide structure class. HREIMS provided a molecular formula of $C_{22}H_{26}O_5$, indicating an isomer of calanolides A-C. The ^{1}H-NMR spectrum of **9** differed from the spectra of calanolides A and B primarily in the D pyran ring resonances, suggesting that the compound was a new stereoisomer of the calanolides. The gross structure and complete ^{1}H- and ^{13}C-NMR assignments of **9** were determined using NMR experiments, including COSY, HMQC, and HMBC. The relative stereochemistry was determined by coupling constant analysis and comparison of **9** with known compounds. The small couplings observed between H10 and H11 (2.0 Hz) and between H12 and H11 (2.0 Hz) suggested that there were no trans-diaxial relationships between neighboring protons. Thus, the molecule must have an axial−equatorial−axial or equatorial−axial−equatorial relationship among H10, H11, and H12. This is the same relative stereochemistry reported for inophyllum D (**10**).[8,9] Indeed, the coupling constants of **9** closely match those reported for **10** (J_{10-11} 2.0, J_{11-12} 2.2 Hz). This provided the gross structure of calanolide F (**9**). The absolute stereochemistry of **9** at C12, determined using the modified Mosher's method,[10,11] was *S*, thus establishing the absolute configuration of **9** as 10*S*, 11*R*, 12*S* (see Figure 1). Esterification of **9** left the coupling constants essentially unchanged, suggesting that the ring conformation was not altered.

We obtained another new coumarin from the latex of *C. teysmannii* during the large-scale purification of (−)-calanolide B.[6] HRFABMS provided a molecular formula of $C_{19}H_{22}O_5$. The ^{1}H-NMR spectrum appeared relatively simple, containing signals for an *n*-propyl group (δ 1.00, t, CH_3; δ 1.60, sextet, CH_2; δ 2.84, t, CH_2), two olefinic methyl groups (δ 1.94, s; δ 1.83, d), two methoxyl groups (δ 3.84, 3.94), and three olefinic/aromatic protons (δ 5.93, s; δ 6.32, s; δ 6.37, q). The ^{13}C-NMR spectrum contained signals for ketone and ester carbonyls (δ 194.3, 160.2), four oxygenated aromatic carbons (δ 159.2, 159.0, 157.5, 153.2), and five additional sp^2 carbons (δ 143.1, 139.3, 111.3, 111.1, 103.9, 91.0), plus signals corresponding to the five methyl groups and the *n*-propyl group methylenes. The gross structure of the compound (**11**) was assembled using HMBC experiments optimized for long-range H−C coupling constants of 8.3 and 5.5 Hz. The methylene protons at δ 2.84 were correlated to the other carbons of the propyl chain along with carbons at δ 157.5, 111.1, and 103.9. The proton on the carbon at δ 111.1 (δ 5.93, H3) was in turn correlated to carbons at δ 38.6 (*n*-propyl CH_2) and δ 157.5, and the ester carbon at δ 160.2. These correlations and chemical shifts were reminiscent of the A ring of the pyranocoumarins of the calanolides. This observation, along with the presence of three additional carbon signals between 150 and 159 ppm, suggested the presence of a coumarin ring system typical of the calanolides. Two of the oxygenated aromatic carbon signals could be accounted for by the two *O*-methyl groups and the third by the lactone of the coumarin ring system. HMBC experiments confirmed this with correlations that placed the *O*-methyl groups at positions 5 and 7 of the coumarin ring. The proton at δ 6.32 (s, carbon δ 91.0) was placed at C6, based on its correlations with C5 (δ 159.2), C7 (δ 159.0), and C4a (δ 103.9). This proton resonance was also correlated to that of the carbon at δ 111.3, which allowed its assignment as C8. The methyl signal at δ 1.83 (C12, δ 15.1) was correlated to the resonances of both remaining olefinic carbons (δ 143.1, 139.3); those carbon resonances were also correlated to the methyl signal at δ 1.94 (C18, δ 10.7). The methyl signal at δ 1.94 was also correlated to the ketone carbonyl resonance at δ 194.3 and required this carbon (C9) to be the final substituent on the coumarin ring at C8. The orientation of the trisubstituted olefin was established as *E* based on the observed NOE enhancements between the methyls at δ 1.94 (H18) and 1.83 (H12) and between the olefinic proton signal at δ 6.37 (H11) and H12 (but not H18), completing assembly of the structure of **11**. This tigloyl side chain has been observed in several of the tricyclic *Calophyllum* pyranocoumarins, for example, calophyllolide (**12**) from *C. inophyllum*.[12]

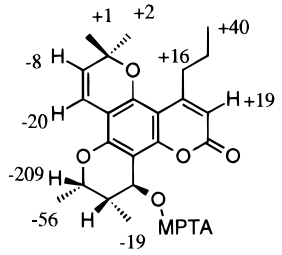


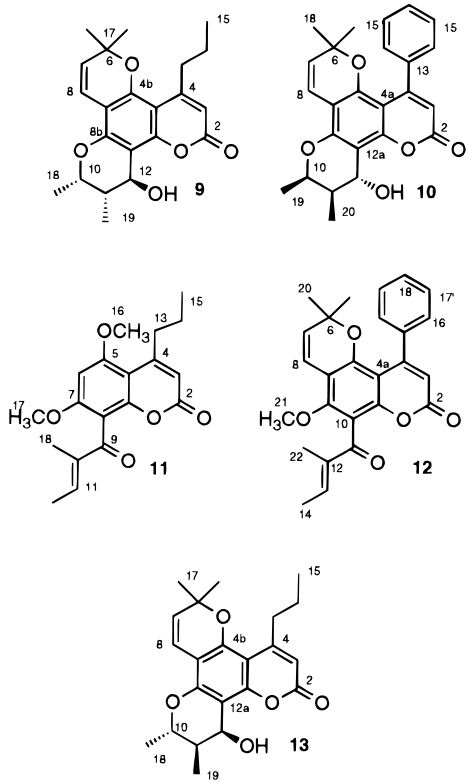
Figure 1. ^{1}H-NMR $\Delta\delta$ values ($\Delta\delta = \delta_S - \delta_R$ in Hertz at 500 MHz) for (R)- and (S)-MPTA esters of calanolide F (**9**).

The newly identified compounds were initially screened for anti-HIV activity in the NCI's primary assay.[13] Those compounds that tested positive were retested in triplicate,[14] using (−)-calanolide B (**13**) as a positive control. The data from these experiments are summarized in Table 3. The observed results fit the patterns of anti-HIV activity observed previously, namely, that the tricyclic (**4**,**5**) and pseudo-type compounds (**6**) are inactive and that the calanolide-type compounds with a 12-β hydroxyl group have anti-HIV activity.

Table 3. Anti-HIV Activities of Compounds **4**, **5**, **6**, **9**, and **11** [(−)-Calanolide B (**13**) Served as a Positive Control]

compound	$EC_{50}\,\mu M$[a]	$IC_{50}\,\mu M$[a]	TI[b]
4	np[c]	2.5	
5	np[c]	14.0	
6	np[c]	2.6	
9	2.84 ± 1.35	12.7 ± 1.0	4.5
11	np[c]	1.0	
13	0.22 ± 0.03	9.8 ± 0.8	44.5

[a] Only those compounds that initally tested positive were tested in triplicate. All other values were determined from a single test. [b] TI is the in vitro "therapeutic index", IC_{50}/EC_{50}. [c] np indicates no protection from HIV-induced cell killing.



Experimental Section

General Experimental Procedures. NMR spectra were recorded on a Varian VXR 500 spectrometer using $CDCl_3$ as solvent and internal standard. IR spectra were measured on a Perkin-Elmer 1600 FTIR spectrometer. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. UV spectra were measured on a Beckman DU-8 spectrophotometer recorded in MeOH or CH_2Cl_2. MS were recorded with a Finnigan MAT 90 spectrometer.

Plant Material. All plant materials were collected under contract for the NCI. The stembark collection of *C. lanigerum* var. *inophylloide* was made by J. S. Burley and B. Lee near Lundu, Sarawak, Malaysia, in October 1987 (voucher: Burley & Lee 0351). The three leaf collections of *C. lanigerum* var. *austrocoriaceum* were made by D. D. Soejarto at the Singapore National Botanical Garden in November 1992 (voucher: Soejarto 1476, 1477, 1478). The leaf and twig collection of *C. teysmannii* var. *inophylloide* was made by D. D. Soejarto from Kuching, Sarawak, in March 1992 (voucher: Soejarto & Mohtar 7872). Herbarium samples are deposited at the Smithsonian Institution, Washington, DC, and the Field Museum, Chicago, IL.

Extraction and Extract Selection. All plant materials were air-dried, ground, and sequentially extracted with 1:1 MeOH−CH_2Cl_2 and MeOH. The extracts were combined and evaporated to generate the organic extract. Extracts were selected for isolation of their pyranocoumarins based on a preliminary analysis of the CH_2Cl_2-soluble materials. The organic extract (200 mg) was dissolved in a minimum of 70% aqueous MeOH and partitioned with CH_2Cl_2 (3 × 50 mL). The CH_2Cl_2 fractions were combined and evaporated to dryness. An ^{1}H-NMR spectrum of the fraction was obtained and analyzed for the presence of pyranocoumarins. Those fractions containing signals indicating the presence of pyranocoumarins were selected for fractionation. Typical procedures for the isolation of pyranocoumarins are exemplified as follows.

Isolation of Compounds from *Calophyllum lanigerum* var. *austrocoriaceum*. A. A 5-g portion of the organic extract of stembark was dissolved in MeOH (75 mL), diluted to a 75% aqueous mixture with H_2O and partitioned with CH_2Cl_2 (3 × 80 mL). The CH_2Cl_2 fractions were combined and evaporated to dryness, *in vacuo*. The CH_2Cl_2-soluble fraction (2.75 g) was eluted from a vacuum−liquid chromatography column (SiO_2, 3 × 5 cm) with hexane−EtOAc mixtures (100% hexane to 100% EtOAc, and a MeOH final rinse). Materials that eluted with hexane−EtOAc (4:1, 307.8 mg) contained the pyranocoumarins. Final purification of the pyranocoumarins was accomplished with HPLC (SiO_2, 7:3 hexanes−EtOAc, 6 mL/min, 1 × 25 cm Rainin Dynamax, UV 270 nm) to yield calanolide E1 (**3**, 198.2 mg, 4.0%) and its diastereomer, calanolide E2 (**4**, 30.0 mg, 0.6%), and calanolide G (**5**, 60.0 mg, 1.2%).

Calanolide E2 (4): $[\alpha]_D$ +79.1° (*c* 0.64, MeOH); UV λ_{max} (CH_2Cl_2) 315 nm (log ϵ 3.94), 301 (3.97), 280 (4.46), 266 (4.40); IR ν_{max} (film) 2964, 2923, 2862, 1703, 1641, 1621, 1580, 1456, 1441, 1385, 1354, 1292, 1236, 1185, 1159, 1144, 1123, 892, 821, 734 cm^{-1}; HRFABMS *m/z* 389.1964 (MH^+, calcd for $C_{22}H_{29}O_6$, 389.1962); FABMS (NOBA) *m/z* 389 (85%), 373 (100), 329 (40), 107 (15), 78 (25); ^{1}H- and ^{13}C-NMR assignments are found in Tables 1 and 2.

Cordatolide E (5): $[\alpha]_D$ + 30.8° (*c* 0.63, MeOH); UV λ_{max} (CH_2Cl_2) 314 nm (log ϵ 3.94), 301 (3.97), 2.80 (4.46), 266 (4.40); IR ν_{max} (film) 2974, 2923, 2872, 1708, 1646, 1653, 1580, 1441, 1385, 1359, 1344, 1287, 1241, 1195, 1154, 1144, 1128, 1113, 1077, 990, 928, 898, 810, 733 cm^{-1}; HRFABMS *m/z* 361.1651 (MH^+, calcd for $C_{20}H_{25}O_6$, 361.1650); FABMS (NOBA) *m/z* 361 (35%), 345 (45), 301 (15), 86 (85) 84 (100), 50 (70); ^{1}H- and ^{13}C-NMR assignments are found in Tables 1 and 2.

B. The organic leaf extract of *C. lanigerum* var. *austrocoriaceum* (2.3g) was partitioned between 80% aqueous MeOH (100 mL) and CCl_4 (3 × 50 mL). The CCl_4-soluble materials (0.496 g) were permeated through a Sephadex LH-20 column (2.5 × 50 cm) with MeOH−CH_2Cl_2 (1:1). Final purification of the coumarin-containing fraction (99 mg) was accomplished with HPLC on Si gel (2.1 × 30 cm, 7:3 hexanes−EtOAc, 25 mL/min) to yield pseudocordatolide C (**6**, 16.7 mg, 0.67%).

Pseudocordatolide C (6): $[\alpha]_D$ +66.8° (*c* 0.6, $CHCl_3$); UV λ_{max} (MeOH) 312 nm (log ϵ 4.11), 273 (4.35), 228 (4.16); IR ν_{max} (film) 2961, 1730, 1660, 1588, 1471, 1361, 1337, 1273, 1219, 1117, 1030, 735 cm^{-1}; HREIMS *m/z* 342.1462 (M^+, calcd for $C_{20}H_{22}O_5$, 342.1467); EIMS *m/z*

342 (4%), 327 (12), 309 (2), 271 (8), 125 (4), 111(8), 97 (14), 83 (13), 71 (14, 69 (15), 57 (24), 18 (100); ^{1}H- and ^{13}C-NMR assignments are found in Tables 1 and 2.

Pyranocoumarins from *Calophyllum teysmannii* var. *inophylloide*. The crude organic extract of leaves and twigs from *C. teysmannii* var. *inophylloide* (2.5 g) was partitioned between 80% aqueous MeOH (150 mL) and CCl_4 (3 × 100 mL). The CCl_4-soluble materials (405 mg) were chromatographed on Sephadex LH-20 (2.5 × 50 cm) and eluted with MeOH−CH_2Cl_2 (1:1). The final purification of the pyranocoumarin-containing fraction was accomplished using HPLC on Si gel (1 × 25 cm, 3:2 hexane−CH_2Cl_2) to yield calanolide F (**9**, 13.4 mg, 0.5%).

Calanolide F (9): $[\alpha]_D$ −51.5° (*c* 0.35, $CHCl_3$); UV λ_{max} (MeOH) 322 nm (log ϵ 4.12), 283 (4.36), 227 (4.35); IR ν_{max} (film) 3449, 2961, 1730, 1658, 1614, 1588, 1469, 1361, 1337, 1277, 1219, 1151, 1116, 1030 cm^{-1}; HREIMS *m/z* 370.1780 (M^+, calcd for $C_{22}H_{26}O_5$, 370.1781); EIMS *m/z* 370 (11%), 355 (40), 352 (63), 337 (100), 309 (15), 299 (8), 265 (5), 251 (5), 176 (6), 147 (12), 120 (6), 91 (4); ^{1}H- and ^{13}C-NMR assignments are found in Tables 1 and 2.

Isolation of compounds from latex of *Calophyllum teysmannii* var *inophylloide*. The crude latex (voucher: Ismawi & Kadushin 004-009) was extracted with CH_2Cl_2; the extract solution was filtered and evaporated to dryness. The resulting crude extract (1.7 g) was partitioned between 90% aqueous MeOH (100 mL) and hexane (3 × 50 mL). The MeOH was adjusted to 80% aqueous MeOH with H_2O and partitioned with CCl_4 (3 × 50 mL). The MeOH fraction was rotary evaporated to remove the MeOH, and the remaining H_2O was frozen and lyophilized. The MeOH fraction (100 mL) was purified by HPLC on Si gel (1 × 25 cm, 7:3 hexane−EtOAc, 10 mL/min) to yield compound (**11**, 15 mg, 0.88%).

Compound 11: UV λ_{max} (MeOH) 318 (log ϵ 4.24), 238 (4.30); IR ν_{max} (film) 3447, 2962, 1730, 1587, 1470, 1361, 1337, 1274, 1219, 1151, 1030, 735 cm^{-1}; HRFABMS *m/z* 330.1467 (MH^+, calcd for $C_{19}H_{22}O_5$, 330.1466); FABMS (NOBA) *m/z* 331 (58%), 310 (4), 275 (24), 247 (6), 219 (2), 133 (4), 84 (6), 76 (10), 33 (100); ^{1}H- and ^{13}C-NMR assignments are found in Tables 1 and 2.

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References and Notes

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