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Phragmalin- and Mexicanolide-Type Limonoids from the Leaves of *Trichilia connaroides*

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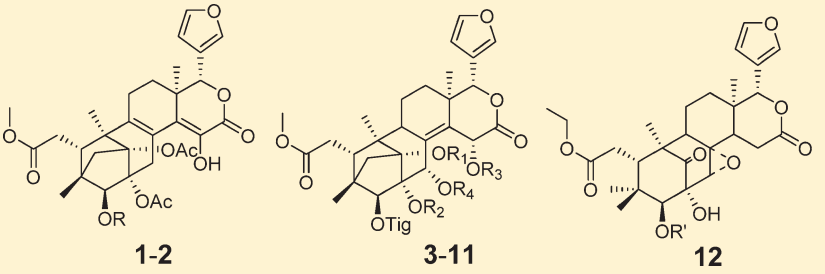
Supporting Information

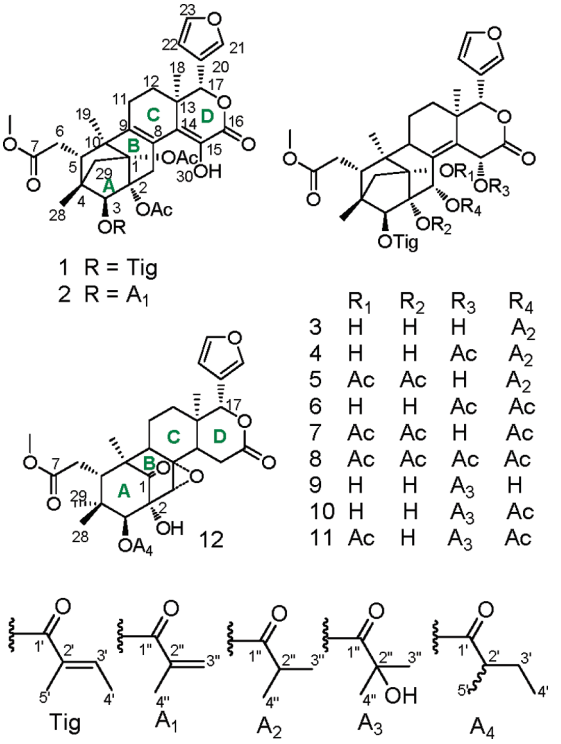
ABSTRACT: Phytochemical investigation of the leaves of *Trichilia connaroides* afforded 12 new limonoids with phragmalin- (**1**−**11**) and mexicanolide-type skeletons (**12**). The structures of these limonoids, including the absolute configuration of **3**, were determined by spectroscopic analysis. Compounds **6** and **8** showed moderate cytotoxicity against HL-60 cells.



The structurally diversified limonoids from plants of the Meliaceae family have been attracting considerable interest.[1] *Trichilia* (Meliaceae) is a genus of trees, widely distributed in Southeast Asia. *Trichilia connaroides* (Wight et Arn.) Bentilezen is known as a traditional medicine for curing arthritis, pharyngitis, tonsillitis, and other ailments in the Yunnan and Guangxi Provinces. Previous phytochemical investigations on this species led to identification of ring C contracted trijugin-type, rearranged 30-nortrijugin-type, and degraded limonoids.[2] To search for structural interesting and bioactive limonoids, chemical investigations of the leaves of *T. connaroides* were performed, revealing 12 new limonoids of the phragmalin (**1**−**11**) and mexicanolide type (**12**). The phragmalins **1** and **2** possess a conjugated vinyl−enol−lactone unit, which is unprecedented in the limonoid family. Herein we report the structural elucidation and the proposed biosynthetic pathways for the formation of **1**−**12**.

RESULTS AND DISCUSSION

Trichagmalin A (**1**) was isolated as a white, amorphous powder, and its molecular formula $C_{36}H_{42}O_{12}$ was established by HRESIMS, requiring 16 degrees of unsaturation. Its NMR data (Tables 1 and 3) revealed a β-furan moiety, five carboxylic carbons, and three double bonds. Since these fragments accounted for only 11 degrees of unsaturation, the remaining unsaturation indicated that **1** is a pentacyclic system. $^1H-^1H$ COSY correlations showed four fragments (Figure 1). In the HMBC spectrum, key correlations of H-30/C-2, 8, 9, H-3/C-2, 5, 29, H-29/C-10, and H-19/C-1, 5, 9, 10 completed a tricyclic [3.3.$1^{2,10}$ 0.$1^{1,4}$]-decane moiety, which is typical in the phragmalin limonoids.[1b] Key HMBC cross-peaks of H$_\beta$-30/C-14 and HO-15/C-14, 15, 16 revealed a conjugated vinyl−enol−lactone unit from C-9 to C-16. Furthermore, the C and D rings were



	R_1	R_2	R_3	R_4
3	H	H	H	A_2
4	H	H	Ac	A_2
5	Ac	Ac	H	A_2
6	H	H	Ac	Ac
7	Ac	Ac	H	Ac
8	Ac	Ac	Ac	Ac
9	H	H	A_3	H
10	H	H	A_3	Ac
11	Ac	H	A_3	Ac

identified by HMBC correlations of H-12/C-9, H-18/C-12, 13, 14, and H-17/C-14. In addition, the β-furan ring attached to C-17, the MeO− at C-7, the tigloyl substituent at C-3, and the

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Table 1. ^{1}H NMR Data of 1−6 in $CDCl_3$

position	1	2	3	4	5	6
3	5.27, s	5.28, s	4.67, s	4.70, s	5.39, s	4.72 s
5	2.39, m	2.39, m	2.85, t,(6.9)	2.88, t (6.7)	2.75, m	2.87, t (7.1)
6	2.52, m	2.54, m	2.32, d, (6.9)	2.33, m	2.30, m	2.33, d (7.1)
	2.52, m	2.54, m	2.32, d, (6.9)	2.33, m	2.30, m	2.33, d (7.1)
9			2.64, d (6.9)	2.73, d (6.8)	2.75, m	2.70, m
11α	2.10, m	2.10, m	1.71, m	1.71, m	1.82, m	1.70, m
11β	2.10, m	2.10, m	1.87, m	1.93, m	1.82, m	1.90, m
12α	1.48, m	1.48, m	1.01, m	1.04, td (13.5, 2.2)	1.26, m	1.03, m
12β	1.30, m	1.29, m	1.38, m	1.40, dt (13.5, 2.2)	1.43, m	1.58, br d (11.0)
15			4.77, s	6.26, d (2.2)	5.26, s	6.23, s
17	5.06, s	5.05, s	5.23, s	5.35, s	5.43, s	5.33, s
18	1.04, s	1.05, s	1.07, s	1.11, s	1.09, s	1.12, s
19	1.04, s	1.04, s	1.12, s	1.14, s	1.14, s	1.14, s
21	7.49, s	7.49, s	7.56, s	7.59, s	7.53, s	7.59, s
22	6.44, s	6.44, br d, (1.0)	6.46, br s	6.48, d (1.2)	6.47, br s	6.47, br s
23	7.44, d (1.5)	7.45, br t, (1.6)	7.40, br s	7.41, d (1.6)	7.42, br s	7.41, br s
28	0.96, s	0.98, s	0.83, s	0.84, s	0.80, s	0.83, s
29a	2.39, m	2.39, m	1.60, d (10.4)	1.57, d (11.0)	2.43, m	1.86, m
29b	2.39, m	2.39, m	1.87[a]	1.87, d (11.0)	2.54, m	1.86, m
30α	2.52[a]	2.54[a]				
30β	4.03, d (18.1)	4.05, d (18.2)	5.75, s	5.41, s	6.55, s	5.36, s
HO-15	6.21, s	6.21, s				
MeO-7	3.63, s	3.64, s	3.71, s	3.73, s	3.66, s	3.72, s
3′	6.89, q (7.1)		7.10, q (6.9)	7.15, dq (7.1, 1.5)	6.66, q (6.7)	7.15, q (6.8)
4′	1.78, d (7.1)		1.75, d (6.9)	1.78, d (7.1)	1.71, d (6.7)	1.77, d (6.8)
5′	1.83, s		1.85, s	2.01, s	1.87, s	1.99, s
2″			2.59, m	2.58, m	2.54, m	
3″		5.59, d (1.6)	1.16, d (6.9)	1.15, d (6.4)	1.17, d (6.48)	
		6.15, s				
4″		1.97, s	1.16, d (6.9)	1.15, d (6.4)	1.17, d (6.48)	
Ac-1	2.03, s	2.05, s			1.97, s	
Ac-2	2.05, s	2.07, s			2.11, s	
Ac-15				2.06, s		2.06, s
Ac-30						2.09, s

[a] Overlapped.

two acetoxy groups at C-1 and C-2 were assigned by relevant HMBC correlations, as shown in Figure 1.

The relative configuration of **1** (Figure 1) was determined by ROESY data. The ROE interaction of H_3-28/H-5 indicated that they are on the same face of ring A and are arbitrarily assigned a β-orientation. ROESY correlations of H-5/$H_β$-30, $H_β$-30/H-3′, and H_3-4′/H-17 indicated that H-17 and the C-3 tigloyl group are also β-orientated, whereas the correlations of H_2-6/H_3-19, H_3-19/H_2-29, and H_3-18/$H_α$-12 suggest α-orientations for H_3-18, H_3-19, and H_2-29.

The ^{1}H and ^{13}C NMR data (Tables 1 and 3) of trichagmalin B (**2**) show similar structural features to those of **1**, although it differs in having a methacryloyl group at C-3, as confirmed by an HMBC cross-peak of H-3/C-1″.

Trichagmalin C (**3**) was assigned a molecular formula of $C_{36}H_{46}O_{12}$ by HRESIMS. ^{1}H, ^{13}C, and DEPT NMR data revealed tigloyl and isobutyryl groups, and the rest are attributed to the phragmalin skeleton, as confirmed by ^{1}H−^{1}H COSY and HMBC correlations (Figure 2). HMBC correlations of H-30/C-8 and 14 and of H-15/C-8 established the C-8/C-14 olefinic bond, and those of H-3/C-1′ and H-30/C-1″ located the tigloyl and isobutyryl substituents at C-3 and C-30, respectively.

The relative configuration of **3** was also identified by ROESY data. The interaction of H_3-28/H-5, H-5/H-17, H-17/H-15, H-17/H-3′, and H-15/H-30 indicated that these protons and the C-3 tigloyl group are all β-oriented, whereas those of H_2-6/H_3-19, H_3-19/H-9, and $H_α$-11/H_3-18 revealed α-orientations for these protons. The absolute configuration of **3** was deduced from the CD spectrum (Figure 3). A prominent positive Cotton effect at 229 nm ($\Delta\varepsilon$ 13.1, $\pi\rightarrow\pi^*$ transition of chromophore **a**) suggested the absolute configuration of **3** as shown according to the CD exciton chirality method.[3] Therefore, the structure of **3** was fully identified, with a $\Delta^{8,14}$ double bond and allylic hydroxyl groups at C-15 and C-30.

Compounds **4**−**11** were identified as analogues of **3** on the basis of their NMR data. Analysis of ^{1}H and ^{13}C NMR data for **4** and **5** (Tables 1 and 3) indicated that one and two *O*-acetyl groups were incorporated in **4** and **5**, respectively. The *O*-acetyl groups were located at C-15 in **4** and at C-1, 2 in **5**, on the basis of corresponding HMBC correlations. Interpretation of ^{1}H and ^{13}C

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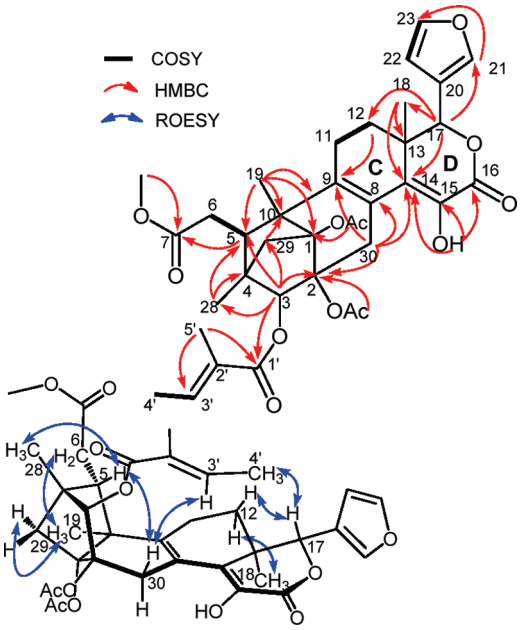

Figure 1. Selected 2D NMR correlations for **1**.

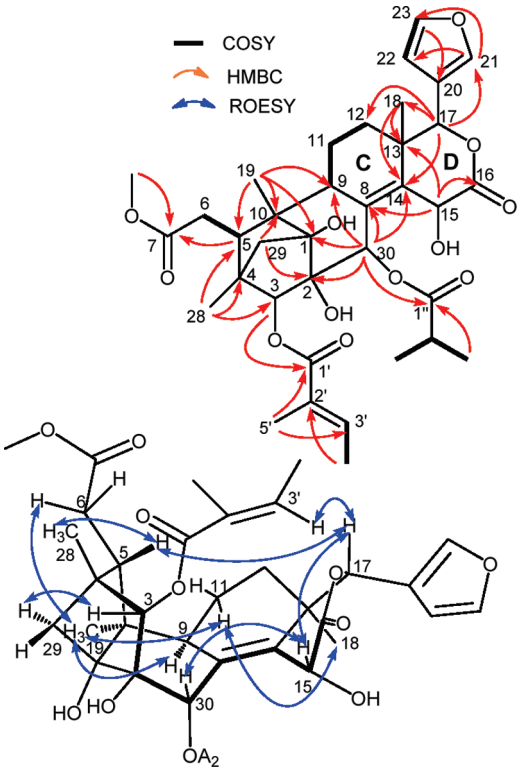

Figure 2. Selected 2D NMR correlations for **3**.

NMR data for **6**−**8** indicated that they share the same framework as **3**, but are devoid of the isobutyryl substituent. The *O*-acetyl groups in **6**−**8** were located as depicted on the basis of corresponding HMBC correlations. The differences in NMR data between **9**−**11** (Tables 2 and 3) and **3** indicate the presence of a hydroxyisobutyroyl group in **9**−**11**. In addition, one and two *O*-acetyl groups were found in **10** and **11**, respectively. The

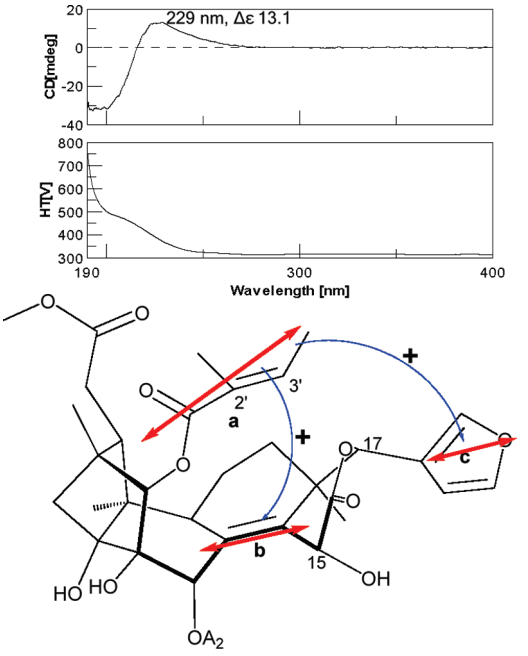

Figure 3. CD spectrum of **3**.

locations of the hydroxyisobutyroyl and *O*-acetyl groups were assigned as shown on the basis of the relevant HMBC data.

Trichanolide (**12**) was isolated as a white, amorphous powder. Its molecular formula $C_{32}H_{42}O_{10}$ was established on the basis of HRESIMS. The NMR data (Tables 2 and 3) revealed a 2-methylbutanoate group and a typical mexicanolide skeleton, as found in ruageanin C.[4] The 2-methylbutanoate group was confirmed by $^1H-^1H$ COSY correlations (H-2′/H-4′ and H-2′/C-5′) and the HMBC cross-peak of H_3-5′/C-1′. It was connected to C-3 by an HMBC cross-peak of H-3/C-1′. The configuration of **3** was deduced to be the same as ruageanin C, on the basis of a comparison of NMR chemical shifts and ROESY correlations.

Two known mexicanolide-type limonoids were also isolated from the same extract and were identified as $\Delta^{8,14}$-2-hydroxy-6-deoxyswietenine[5] and ruageanin B[4] on the basis of comparison of their NMR and ESIMS data with those reported.

The phragmalins were proposed to be biosynthetically derived from mexicanolide-type limonoids through a radical intermediate.[6,7] However, this pathway requires an oxy-substituent at C-9 as a result of radical termination. The coexistence of the phragmalin and mexicanolide limonoids in *T. connaroides* further supported their close biogenetic relationship (Scheme 1). Since the oxy-substituent at C-9 in the phragmalins **1**−**11** is absent, the biogenetic pathway should be different from the radical pathways. The mexicanolide-type compound **13** might undergo a Norrish II reaction,[8] to afford a phragmalin-type intermediate i, which may prevent formation of the oxy-substituent at C-9. Subsequently, the allylic oxidation of the intermediate i may yield phragmalins **1** and **3**. Compounds **4**−**11**, as analogues of **3**, could form via transesterification.

Compounds **1**, **3**, **6**−**8**, **10**, **11**, and ruageanin B were evaluated for cytotoxicity against the human tumor cell lines HL-60, SMMC-7721, A-549, MCF-7, and SW-480, using cisplatin as the positive control. Compounds **6** and **8** showed moderate cytotoxicity against HL-60 cells, with IC_{50} values of 17.05 and 21.01 μM, respectively.

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Table 2. ^{1}H NMR Data of 7 and 8 in Acetone-d_6 and 9−12 in $CDCl_3$

position	7	8	9	10	11	12
3	5.35, s	5.32, s	4.74, s	4.71, s	4.70, s	5.13, s
5	2.81, dd (17.0, 6.8)	2.86, m	2.87, m	2.86, m	2.81, t (7.3)	3.14, br d (7.3)
6	2.45, m	2.41, d (3.5)	2.32, m	2.33, m	2.32, m	2.34, m
6	2.55, m	2.56, m	2.32, m	2.33, m	2.32, m	2.34, m
9	2.90, m	2.8, d, (12.1)	2.62, d (6.6)	2.73, d (7.09)	2.74, m	1.88, m
11	1.97, m	1.72, m	1.71, m	1.71, m	1.69, m	1.83, m
11	1.75, m	2.00, m	1.88, m	1.88, m	1.85, m	
12	1.05, m	0.98, m	1.04, m	1.07, td (13.7, 3.1)	1.11, m	1.96, m
12	1.48, dt (13.7, 2.7)	1.47, m	1.42, m	1.44, m	1.43, m	1.21, m
14						1.65, m
15	5.17, br s	6.59[a]	6.13, s	6.26, d (1.96)	6.26, d (1.7)	3.63, m
						2.87, dd (15.9, 3.9)
17	5.44, s	5.46, s	5.28, s	5.38, s	5.37, s	5.18, s
18	1.09, s	1.04, s	1.13, s	1.13, s	1.14, s	1.01, s
19	1.16, s	1.13, s	1.12, s	1.14, s	1.07, s	1.17, s
21	7.64, s	7.63, s	7.57, s	7.58, s	7.58, s	7.49, s
22	6.56, br d (1.0)	6.54, s	6.47, br s	6.47, d (1.2)	6.46, d (1.2)	6.46, br s
23	7.60, br d (1.5)	7.57, s	7.42, br s	7.41, br t (1.6)	7.41, br t (1.6)	7.44, br s
28	0.76, s	0.73, s	0.84, s	0.83, s	0.88, s	0.76, s
29a	2.55, m	2.48, m	1.65, m	1.60, d (11.0)	2.41, m	0.80, s
29b	2.55, m	2.48, m	1.83, m	1.88, m	2.52, m	
30β	6.59, s	6.09, s	3.99, s	5.48, s	5.48, s	3.56, s
HO-15	4.92, d (2.3)					
MeO-7	3.68, s	3.67, s	3.72, s	3.72, s	3.73, s	3.73, s
2′						2.62, m
3′	6.69, m	6.59, m	7.12, q (6.8)	7.12, dq (7.1, 1.5)	7.11, dq (7.0, 1.1)	1.61, m
						1.80, m
4′	1.68, d (6.8)	1.61, d (6.6)	1.76, d (6.8)	1.76, d (7.1)	1.76, d (7.0)	1.00, t (8.2)
5′	1.80, s	1.87, s	1.93, s	1.98, s	1.99, s	1.27, d (6.9)
3″			1.52, s	1.50, s	1.51, s	
4″			1.48, s	1.38, s	1.38, s	
Ac-1	2.08, s	1.76, s			2.05, s	
Ac-2	2.11, s	2.04, s				
Ac-15		1.92, s				
Ac-30	1.91, s	2.02, s		2.07, s	2.07, s	

[a] Overlapped.

EXPERIMENTAL SECTION

General Experimental Procedures. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-400 spectrometer, and the 2D NMR spectra were recorded on a Bruker DRX-500 instrument. Chemical shifts were calculated using TMS as the internal standard. ESIMS and HRESIMS spectra were measured with a Finnigan MAT 90 instrument. Optical rotations were measured with a Perkin-Elmer model 241 polarimeter. CD spectra were obtained on a JASCO J-810 spectrophotometer. IR spectra were recorded on a Bio-Rad FTS-135 spectrometer with a KBr disk. UV spectra were recorded on a Shimadzu UV-210A. Column chromatography was performed on silica gel (90−150 μm; Qingdao Marine Chemical Inc., Qingdao, China), MCI gel (75−150 μm; Mitsubishi Chemical Corporation, Tokyo, Japan), Sephadex LH-20 (40−70 μm; Amersham Pharmacia Biotech AB, Uppsala, Sweden), and Lichroprep RP-18 gel (40−63 μm; Merck, Darmstadt, Germany). Semipreparative HPLC was performed on a Chromolith semipreparative RP-18e column (i.d. 10.0 × 100 mm; Merck Co. Ltd., USA). Precoated silica gel GF_{254} and HF_{254} plates (Qingdao Marine Chemical Inc., Qingdao, China) were used for thin-layer chromatography (TLC).

Plant Material. The leaves of *T. connaroides* were collected from Wenshan, Yunnan Province, People's Republic of China, in October 2008. The plant was identified by Prof. Jingyun Cui of the Xishuangbanna Tropical Botanical Garden, Chinese Academy of Sciences. A voucher specimen (No. KUN0620839) was deposited at the Kunming Institute of Botany, CAS.

Extraction and Isolation. The air-dried powder of the plant material (30 kg) was extracted three times with MeOH. The extracts were combined and concentrated (620 g), then dispersed onto 1.0 kg of silica gel. It was sequentially eluted with petroleum ether, $CHCl_3$, EtOAc, and acetone. The EtOAc fraction (150 g) was chromatographed on a MCI column and then a C_{18} column, eluting with 20%−100% MeOH. The fractions eluted with 60% (fraction A, 32 g) and 80% MeOH (fraction B, 65 g) were found to contain limonoids by TLC analysis. Fraction A was further separated by silica gel column chromatography using $CHCl_3$−acetone gradient elution to afford six fractions. Each fraction was separated by Sephadex LH-20 (90% MeOH) and further purified by semipreparative RP

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Table 3. ^{13}C NMR Data for 1−12 (7 and 8 in acetone-d_6, the others in $CDCl_3$)

position	1	2	3	4	5	6	7	8	9	10	11	12
1	85.3	85.2	83.6	83.6	88.4	83.6	89.1	89.2	84.1	83.7	89.0	213.2
2	85.4	85.4	76.5	76.9	83.5	76.8	84.5	84.3	76.6	76.9	77.7	78.0
3	81.3	81.5	88.7	88.3	82.3	88.1	83.4	82.8	87.1	88.2	87.8	84.3
4	45.5	45.6	43.0	43.0	45.8	43.0	46.7	46.6	43.3	43.0	44.1	39.8
5	42.9	42.9	37.4	37.5	35.8	37.4	36.5	36.5	37.5	37.5	36.0	42.4
6	39.0	39.1	33.6	33.7	33.7	33.6	33.9	33.8	33.7	33.6	33.6	32.8
7	173.4	173.4	174.1	174.2	173.7	174.2	175.3	175.6	174.2	174.2	173.9	173.9
8	120.8	120.8	133.5	135.7	131.8	134.5	133.0	132.8	138.8	135.8	135.2	63.0
9	141.3	141.6	34.2	34.0	35.8	35.7	36.7	36.7	34.7	36.0	36.4	55.3
10	49.4	49.4	47.3	47.5	49.7	47.4	50.7	50.9	47.7	47.4	49.2	49.0
11	23.2	23.3	18.3	18.3	18.4	18.2	18.9	18.7	18.1	18.2	18.2	19.2
12	30.8	30.8	28.5	28.4	29.0	28.2	29.7	29.5	28.5	28.5	28.5	33.3
13	37.7	37.8	38.5	39.0	38.1	39.0	38.8	39.8	38.5	38.7	38.3	36.3
14	126.5	126.4	138.9	134.7	140.6	135.7	141.2	136.7	134.0	135.2	135.6	45.5
15	133.5	133.6	64.3	64.2	64.3	64.2	65.2	65.8	64.5	64.5	64.4	33.7
16	166.0	166.1	172.7	168.4	171.7	167.7	171.9	168.4	167.2	167.2	167.1	171.6
17	81.3	81.3	80.9	80.4	80.2	80.4	80.8	80.5	81.1	80.5	80.4	78.7
18	16.6	17.0	16.7	16.7	17.5	16.6	17.9	17.4	16.5	16.8	16.8	26.3
19	16.6	16.7	17.3	17.3	17.9	17.3	18.0	18.1	17.6	17.3	18.0	16.0
20	119.7	119.7	120.4	120.4	120.6	120.4	122.1	121.8	120.4	120.4	120.3	120.0
21	141.7	141.4	141.8	142.0	141.8	142.0	142.8	143.0	141.9	142.1	142.1	140.9
22	109.9	110.0	109.8	109.9	110.0	109.8	110.9	110.9	109.8	109.8	109.8	110.2
23	143.1	143.1	142.9	143.0	143.0	143	144.2	144.4	143.1	143.0	143.1	143.1
28	16.9	16.6	14.8	14.8	14.5	14.7	15.0	15.1	14.8	14.5	14.8	21.6
29	33.7	33.7	39.6	39.8	38.8	39.7	39.4	39.3	39.3	39.7	38.7	20.3
30	29.3	29.3	70.8	69.6	67.6	70.1	68.7	68.3	68.5	70.2	69.7	67.5
MeO-7	51.8	51.9	51.9	52.0	52.0	52.0	52.3	52.4	51.9	52.0	52.1	52.4
1′	166.4		168.4	167.7	167.5	168.4	167.9	168.0	168.3	168.6	168.3	175.5
2′	128.1		128.6	129.8	130.2	129.8	130.9	134.7	129.5	129.7	129.7	41.3
3′	137.9		140.1	139.2	135.4	139.3	135.2	132.1	139.3	139.5	139.4	26.8
4′	14.5		14.5	14.5	13.8	14.5	13.9	13.6	14.5	14.8	14.5	11.8
5′	12.1		12.1	12.1	13.0	12.2	13.1	13.3	12.2	12.2	12.2	17.2
1″		165.8	178.4	176.8	176.0				174.6	174.8	174.6	
2″		135.9	35.7	35.8	34.4				72.5	72.5	72.4	
3″		18.4	19.0	19.2	19.0				26.9	26.8	26.8	
4″		126.1	18.6	18.5	18.9				26.4	27.1	27.2	
Ac-1	169.5	169.5			168.4		169.9	169.3			170.1	
	21.9	21.9			21.5		21.6	21.1			21.9	
Ac-2	170.0	170.0			169.4		170.5	169.8				
	21.8	21.9			22.0		22.0	22.0				
Ac-15				169.6		169.6		169.3				
				21.0		20.9		21.3				
Ac-30						171.0	168.9	168.5		171.6	171.0	
						21.2	21.3	21.4		21.4	21.4	

HPLC eluting with 63%−67% MeOH to afford **2** (7 mg), **8** (45 mg), **9** (5 mg), **10** (17 mg), **11** (18 mg), $\Delta^{8,14}$-2-hydroxy-6-deoxyswietenine (4 mg), and ruageanin B (22 mg). Fraction B was processed under the same chromatographic conditions to afford **1** (24 mg), **3** (40 mg), **4** (4 mg), **5** (60 mg), **6** (50 mg), **7** (13 mg), and **12** (10 mg).

Trichagmalin A (***1***)*:*. white powder; $[\alpha]^{27}_D$ +202 (*c* 0.35, MeOH); CD (MeOH) λ_{max} ($\Delta\varepsilon$) 224 nm (−5.2), 303 (+21.1); UV (MeOH) λ_{max} 213.2, 310.4 nm; IR (KBr) ν_{max} 3442, 1739, 1710, 1648, 1639, 1628, 1371, 1243 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 3; HRESIMS *m*/*z* 689.2578 (calcd for $C_{36}H_{42}O_{12}Na$, 689.2573).

Trichagmalin B (***2***)*:*. white powder; $[\alpha]^{27}_D$ +192 (*c* 0.48, MeOH); UV (MeOH) λ_{max} 310.4, 208.6 nm; IR (KBr) ν_{max} 3435, 1737, 1708, 1629, 1244, 1227, 1158 cm^{-1}; ^1H and ^{13}C NMR, see Tables 1 and 3; HRESIMS *m*/*z* 675.2409 (calcd for $C_{35}H_{40}O_{12}Na$, 675.2417).

Trichagmalin C (***3***)*:*. white powder; $[\alpha]^{27}_D$ −62 (*c* 0.65, MeOH); CD (MeOH) λ_{max} ($\Delta\varepsilon$) 193 nm (−33.0), 229 (+13.1); UV (MeOH) 212 nm; IR (KBr) ν_{max} 3450, 1728, 1706, 1643, 1266, 1200 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 3; HRESIMS *m*/*z* 693.2877 (calcd for $C_{36}H_{46}O_{12}Na$, 693.2886).

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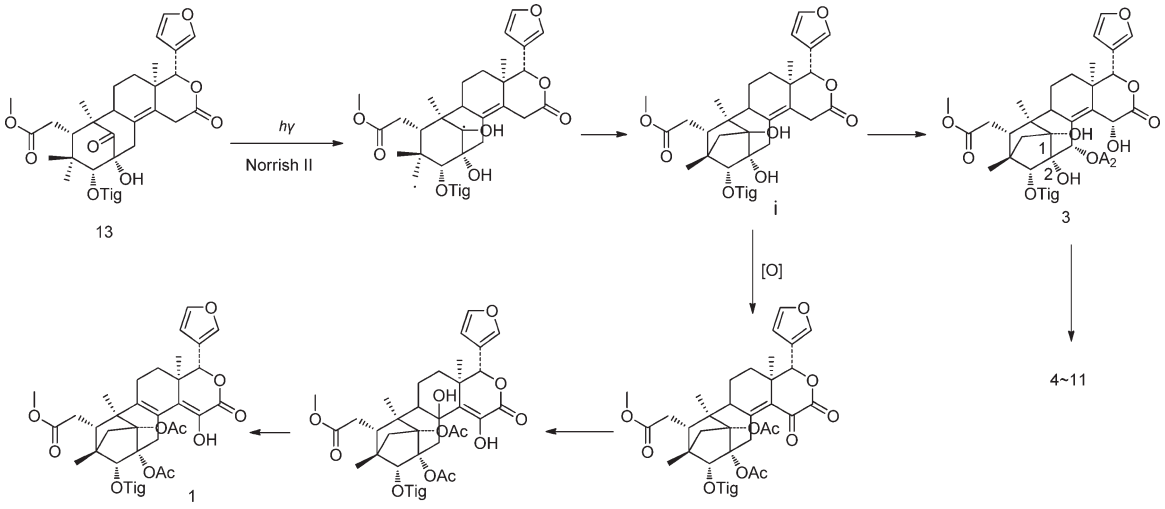
Scheme 1. Plausible Biogenetic Pathways for the Formation of Phragmalin-Type Limonoids from *T. connaroides*



*15-Acetyltrichagmalin C (**4**)*:. white powder; $[\alpha]^{27}_{D}$ −39 (*c* 0.38, MeOH); IR (KBr) ν_{max} 3445, 1766, 1752, 1736, 1697, 1275, 1197 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 3; HRESIMS *m/z* 735.2975 (calcd for $C_{38}H_{48}O_{13}Na$, 735.2992).

*1,2-Diacetyltrichagmalin C (**5**)*:. white powder; $[\alpha]^{27}_{D}$ −26 (*c* 0.77, MeOH); IR (KBr) ν_{max} 3437, 1750, 1730, 1629, 1367, 1241, 1040 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 3; HRESIMS *m/z* 777.3108 (calcd for $C_{40}H_{50}O_{14}Na$, 777.3098).

*Trichagmalin D (**6**)*:. white powder; $[\alpha]^{28}_{D}$ −42 (*c* 0.37, MeOH); IR (KBr) ν_{max} 3465, 1760, 1753, 1370, 1231, 1195, 1045, 1023 cm^{-1}; ^{1}H and ^{3}C NMR data, see Tables 1 and 3; HRESIMS *m/z* 707.2671 (calcd for $C_{36}H_{44}O_{13}Na$, 707.2679).

*Trichagmalin E (**7**)*:. white powder; $[\alpha]^{27}_{D}$ −32 (*c* 0.65, MeOH); IR (KBr) ν_{max} 3437, 1751, 1730, 1629, 1370, 1250, 1039 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 3; HRESIMS *m/z* 749.2802 (calcd for $C_{38}H_{46}O_{14}Na$, 749.2785).

*15-Acetyltrichagmalin E (**8**)*:. white powder; $[\alpha]^{27}_{D}$ −30 (*c* 0.63, MeOH); IR (KBr) ν_{max} 1768, 1750, 1640, 1370, 1250, 1193, 1044 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 3; HRESIMS *m/z* 791.2914 (calcd for $C_{40}H_{48}O_{15}Na$, 791.2890).

*Trichagmalin F (**9**)*:. white powder; $[\alpha]^{28}_{D}$ −12 (*c* 0.29, MeOH); IR (KBr) ν_{max} 3439, 1756, 1728, 1461, 1269, 1197, 1135, 1026 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 3; HRESIMS *m/z* 709.2839 (calcd for $C_{36}H_{46}O_{13}Na$, 709.2836).

*30-Acetyltrichagmalin F (**10**)*:. white powder; $[\alpha]^{28}_{D}$ −39 (*c* 0.27, MeOH); IR (KBr) ν_{max} 3450, 1760, 1727,1461, 1381, 1233, 1130, 1026 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 3; HRESIMS *m/z* 751.2953 (calcd for $C_{38}H_{48}O_{14}Na$, 751.2941).

*1,30-Diacetyltrichagmalin F (**11**)*:. white powder; $[\alpha]^{28}_{D}$ −39 (*c* 0.24, MeOH); IR (KBr) ν_{max} 3442, 1759, 1726, 1461, 1437, 1373, 1235, 1122, 1028 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 3; HRESIMS *m/z* 793.3030 (calcd for $C_{40}H_{50}O_{15}Na$, 793.3047).

*Trichanolide (**12**)*:. white powder; $[\alpha]^{27}_{D}$ −44 (*c* 0.41, MeOH); IR (KBr) ν_{max} 3441, 1737, 1629, 14601, 1139, 1026 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 3; HRESIMS *m/z* 609.2694 (calcd for $C_{32}H_{42}O_{10}Na$, 609.2675).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information. 1D and 2D NMR spectra of compounds **1**−**12**. This material is available free of charge via the Internet at http://pubs.acs.org.

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