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Two Diastereomeric Triterpene-Lignan Esters Having Dimeric Structure and Their Biosynthetically Related Triterpene Caffeate from *Rhoiptelea chiliantha*

Zhi-Hong Jiang

College of Traditional Chinese Pharmacy, China Pharmaceutical University,
Tong Jia Xiang, Nanjing 210009, China

Takashi Tanaka and Isao Kouno*

Faculty of Pharmaceutical Sciences, Nagasaki University,
Bunkyo-machi, Nagasaki 852, Japan

Abstract: 27-Caffeoyloxy-3-β-hydroxyolean-12-en-28-oic acid (1) and rhoipteleic acids A (2) and B (3), diastereomeric esters composed of two triterpene units and enantiomeric lignan carboxylic acids, were isolated from the bark of *Rhoiptelea chiliantha*. The structures have been determined on the basis of spectroscopic and chemical evidence including biomimetic synthesis of 2 and 3 from 1.

The Rhoipteleaceae is a monotypic family including only one genus and one species, *i.e. Rhoiptelea chiliantha* Diels et Hand.-Mazz., which is distributed in southern part of China and northern Vietnum. From the point of chemotaxonomical view, we have been interested in the chemical constituents of this plant, and now isolated a new triterpene caffeate (**1**) and two novel triterpene-lignan esters having dimeric structure (**2** and **3**) from the bark. This report describes the isolation and structure elucidation of these metabolites.

The EtOH extract of the air-dried bark (4.5kg) was partitioned between H_2O and ether. The ether layer was treated with MeOH, and the MeOH soluble portion was chromatographed over MCI-gel CHP 20P with 90% MeOH. The fractions positive to 2% $FeCl_3$-EtOH reagent were further fractionated by silica gel chromatography ($CHCl_3$-MeOH) to give two fractions. The first fraction was purified by ODS chromatography (80% MeOH) to give **1**. The second fraction was also chromatographed over ODS (80% MeOH) , and purified by preparative HPLC (ODS, 90% MeOH) to give **2** and **3**. The yields of the compounds **1**, **2** and **3** were 0.4, 0.03 and 0.03%, respectively, based on dry weight.

Compound **1**, colorless needles from 80% MeOH, mp 225-226°C, $C_{39}H_{54}O_7$, $[\alpha]_D$ +130.9° (*c* 0.5, MeOH), FAB-MS *m/z* 727 $[M+H+glycerol]^+$, showed dark green colorlation with $FeCl_3$ reagent. The ^{13}C-NMR spectrum (Table 2) indicated the presence of caffeoyl group, which was confirmed by methanolysis (HCl-MeOH) of trimethylate of **1** giving methyl *trans*-3,4-dimethoxycinnamate.

Alkaline hydrolysis (5% NaOH-MeOH, 1:2 v/v) of **1** gave a triterpene **1a**. **1a** was identified as 3, 27-dihydroxy-12-oleanen-28-oic acid,[1a] which has so far been found in a few plants, as far as we know.[1] The location of the caffeoyl group in **1** was determined to be at C-27 hydroxyl group on the basis of the downfield shifts of H-27 [δ 4.42 and 4.12, Δδ +0.23 and 0.3] and C-27 (Table I) compared with those of **1a**. Accordingly, **1** was concluded to be 27-caffeoyloxy-3β-hydroxyolean-12-en-28-oic acid.

Rhoipteleic acids A (**2**), a white powder, $C_{78}H_{106}O_{14}$, $[\alpha]_D$ +86.9° (*c* 0.5, MeOH), and B (**3**), white powder, $C_{78}H_{106}O_{14}$, $[\alpha]_D$ +49.4° (*c* 0.5, MeOH), were shown to have the same constitution by

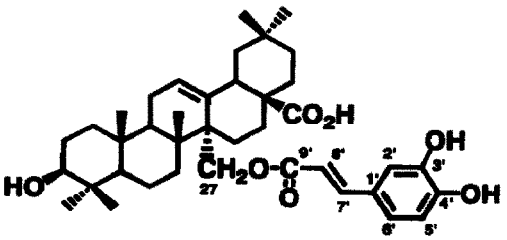
FAB-MS [m/z 1267 $[M+H]^+$]. The presence of triterpene framework in each molecule was suggested by the ^{13}C-NMR signals (Table I), whose chemical shifts were closely related to those of **1**. Furthermore, each carbon resonance due to triterpene unit appeared in pairs. Taking into account of the molecular masses of these compounds, this observation indicated that **2** and **3** have two triterpene units. On alkaline hydrolysis, both of **2** and **3** yielded a single triterpene **1a**.

Table 1. ^{13}C-NMR Spectral Data for **1a** and Triterpene Moieties of **1**, **2** and **3**

	1a[a]	**1**[a]	**2**[b]	**3**[b]		**1a**	**1**	**2**	**3**
C-1	38.9 (t)	39.0 (t)	39.4 (t)	40.6 (t)	C-16	23.8 (t)	23.6 (t)	23.7 (t)	24.5 (t)
			40.1 (t)	41.2 (t)				23.8 (t)	24.7 (t)
C-2	28.1 (t)	28.0 (t)	27.8 (t)x2	28.5 (t)	C-17	46.6 (s)	46.5 (s)	47.2 (s)	48.1 (s)
			-	28.7 (t)				47.4 (s)	48.3 (s)
C-3	78.1 (d)	77.9 (d)	79.7 (d)x2	80.4 (d)x2	C-18	41.8 (d)	41.9 (d)	42.1 (d)	43.3 (d)
			-	-				42.4 (d)	43.5 (d)
C-4	39.4 (s)	39.3 (s)	39.9 (s)x2	40.6 (s)	C-19	45.6 (t)	45.4 (t)	45.1 (t)	46.1 (t)
			-	40.8 (s)				45.4 (t)	46.3 (t)
C-5	55.8 (d)	55.8 (d)	56.9 (d)	57.4 (d)	C-20	31.0 (s)	30.9 (s)	31.3 (s)	32.1 (s)
			57.1 (d)	57.9 (d)				31.6 (s)	32.3 (s)
C-6	18.9 (t)	18.8 (t)	19.4 (t)x2	20.26 (t)	C-21	33.7 (t)	33.7 (t)	34.3 (t)*	35.0 (t)#
			-	20.34 (t)				34.9 (t)*	35.7 (t)#
C-7	34.1 (t)	34.1 (t)	34.9 (t)*	35.7 (t)x2#	C-22	33.2 (t)	33.1 (t)	33.7 (t)x2	34.5 (t)x2
			35.0 (t)*	-				-	-
C-8	40.5 (s)	40.5 (s)	41.06 (s)	41.9 (s)x2	C-23	28.7 (q)	28.7 (q)	28.9 (q)	29.5 (q)
			41.14 (s)	-				29.1 (q)	29.8 (q)
C-9	48.8 (d)	49.1 (d)	50.1 (d)	50.85 (d)	C-24	16.0 (q)	15.8 (q)	16.3 (q)x2	17.1 (q)$
			50.4 (d)	50.90 (d)				-	17.2 (q)$
C-10	37.6 (s)	37.6 (s)	38.3 (s)x2	39.1 (s)	C-25	16.5 (q)	16.5 (q)	16.3 (q)	17.2 (q)$
			-	39.3 (s)				16.5 (q)	17.3 (q)$
C-11	24.1 (t)	24.1 (t)	24.7(t)x2	25.86 (t)*	C-26	18.8 (q)	18.6 (q)	18.8 (q)	19.56 (q)
			-	25.94 (t)*				18.9 (q)	19.64 (q)
C-12	127.7 (d)	127.0 (d)	128.2 (d)	128.9 (d)	C-27	64.5 (t)	66.1 (t)	67.2 (t)	67.1 (t)
			128.7 (d)	129.1 (d)				67.4 (t)	67.6 (t)
C-13	139.9 (s)	138.9 (s)	137.5 (s)	138.9 (s)	C-28	180.2 (s)	180.1 (s)	181.7 (s)x2	182.4 (s)
			137.9 (s)	139.6 (s)				-	182.5 (s)
C-14	48.0 (s)	48.0 (s)	46.7 (s)	47.4 (s)	C-29	33.2 (q)	33.2 (q)	33.2 (q)	33.9 (q)
			46.9 (s)	47.7 (s)				33.5 (q)	34.2 (q)
C-15	24.4 (t)	24.4 (s)	25.1 (t)	25.9 (t)*	C-30	23.9 (q)	23.2 (q)	23.6 (q)	24.4 (q)
			25.5 (t)	26.1 (t)*				23.8 (q)	24.9 (q)

a 100MHz, pyridine-d_5. *b* 100MHz, methanol-d_4.

*, #, $: Assignments may be interchanged in each column.



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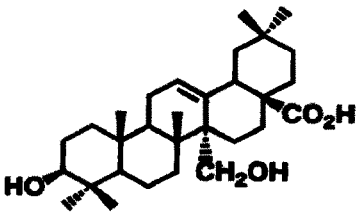


1a

Table 2. ^{13}C-NMR Spectral Data for Phenol Carboxylic Acid Moieties of 1, 2 and 3

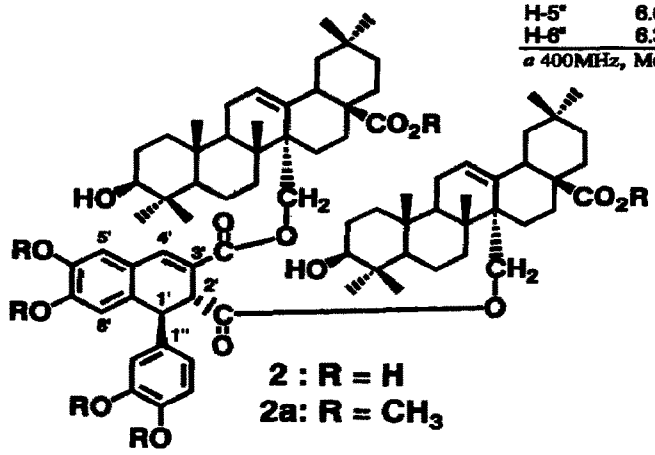
	1[a]	2[b]	3[b]
C-1'	126.6 (s)	47.1 (d)	47.4 (d)
C-2'	115.9 (d)*	49.9 (d)	50.5 (d)
C-3'	147.7 (s)	130.6 (s)	131.9 (s)
C-4'	150.5 (s)	140.4 (d)	140.8 (d)
C-4a'	-	136.4 (s)	137.6 (s)
C-5'	116.8 (d)*	116.9 (d)*	117.9 (d)*
C-6'	121.8 (d)	145.9 (s)#	146.8 (s)#
C-7'	145.7 (d)	149.1 (s)	150.1 (s)
C-8'	115.4 (d)*	117.9 (d)*	118.3 (d)*
C-8a'	-	125.6 (s)	125.9 (s)
C-9'	167.2 (s)	-	-
C-1"	-	122.1 (s)	123.7 (s)
C-2"	-	116.0 (d)*	116.5 (d)*
C-3"	-	144.8 (s)#	145.8 (s)#
C-4"	-	146.1 (s)#	147.0 (s)#
C-5"	-	116.3 (d)*	117.0 (d)*
C-6"	-	119.8 (d)	120.4 (d)
2-COO	-	174.7 (s)	174.4 (s)
3-COO	-	168.4 (s)	169.3 (s)

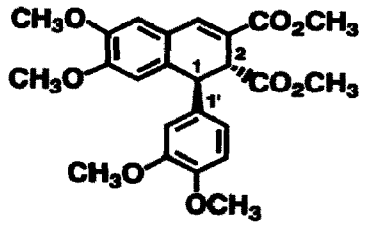
a 100MHz, pyridine-d_5. *b* 100MHz, methanol-d_4.
*, #: Assignments may be interchanged in each column.

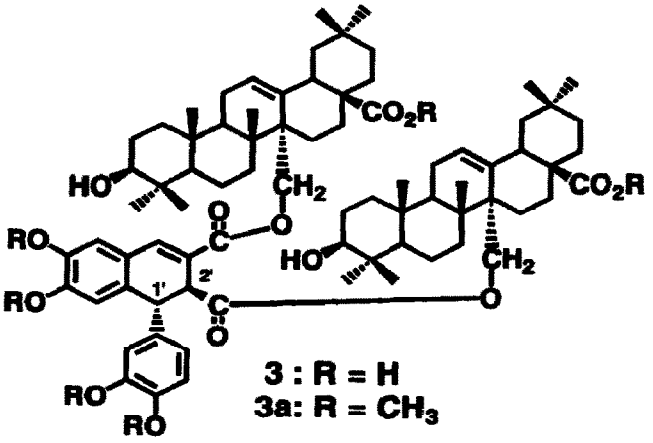
Table 3. ^{1}H-NMR Spectral Data for 2 and 3[a]

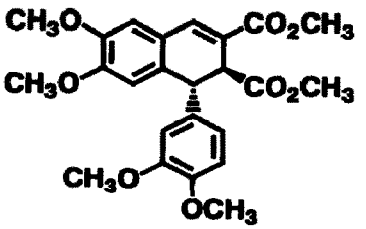
	2	3
Triterpene units		
H-3	3.17 (2H, m)	3.08 (dd, J=7, 10)
	-	3.21 (dd, J=5,11)
H-18	2.68 (2H, m)	2.82 (2H, m)
H-27	4.10 (d, J=13)	3.99 (d, J=12)
	4.17 (d, J=12)	4.13 (d, J=13)
	4.30 (d, J=12)	4.28 (d, J=13)
	4.34 (d, J=13)	4.40 (d, J=12)
H-12	5.26 (t, J=3)	5.51 (t, J=3)
	5.45 (t, J=3)	5.60 (br s)
CH_3	0.99, 0.96,	1.01, 0.98,
	0.95, 0.91 (x2),	0.96, 0.904,
	0.86, 0.79,	0.900, 0.81,
	0.77, 0.76 (x2),	0.80, 0.79,
	0.74, 0.62	0.78, 0.75,
		0.71, 0.57
lignan unit		
H-1'	4.50 (br s)	4.48 (br s)
H-2'	3.82 (d, J=2)	3.76 (d, J=1)
H-4'	7.61 (s)	7.61 (s)
H-5'	6.85 (s)	6.80 (s)
H-8'	6.49 (s)	6.53 (s)
H-2"	6.27 (d, J=2)	6.37 (d, J=2)
H-5"	6.62 (d, J=8)	6.59 (d, J=8)
H-6"	6.32 (dd, J=2, 8)	6.41 (dd, J=2, 8)

a 400MHz, MeOH-d_4. *J* values are expressed in Hz.









The remaining part of the molecules of **2** and **3** were considered to be phenol carboxylic acid moieties, because of the dark green colorlation of these compounds with $FeCl_3$ reagent, and the appearance of the ^{13}C-NMR signals listed in Table II, including the carbon signals due to two aromatic rings and conjugated and non-conjugated carboxyl groups. The chemical shifts of these carbons and the appearance of the spin systems due to catechol ring (H-5", H-6", H-2"), three one-proton singlets (H-4', H-5', H-8'), and a pair of aliphatic proton signals (H-1', H-2') in each ^1H-NMR spectrum (Table III), suggested the presence of 1, 2-dihydro-1-(3', 4'-dihydroxyphenyl)-6, 7-dihydroxynaphthalene-2, 3-dicarboxylic acid[2] moiety in the molecule. On methylation (CH_2N_2), **2** and **3** gave hexamethylates **2a** and **3a**, which were successively hydrolyzed (*p*-TsOH in benzene[3]) and methylated (CH_2N_2) to give dimethyl esters **2b** and **3b** [**2b** and **3b**: EI-MS *m/z* 442 (M^+)], respectively. The ^1H-NMR spectra of these compounds were completely superimposable, and identical to those of dimethyl 1, 2-dihydro-1-(3, 4-dimethoxyphenyl)-6, 7-dimethoxynaphthalene-2, 3-dicarboxylate.[2a] Furthermore, the $[\alpha]_D$ value of **2b** [+146.8° (*c* 0.3, $CHCl_3$)] and **3b** [-72.9° (*c* 0.3, $CHCl_3$)[4]] indicated that **3b** has an antipodal structure of **2b**, and the positive value of **2b** showed that the absolute configurations at C-1 and C-2 of **2b** are *R* and *S*, respectively.[2a]

The locations of the ester linkage in **2** and **3** were concluded to be C-27 hydroxyl group of both triterpene unit, on the basis of the down field shifts of H-27 (Table III) and C-27 (Table I) compared with those of **1a**. From these results, the structures **2** and **3** were assigned to rhoipteleic acids A and B, respectively.

Because rhoipteleic acids A (**2**) and B (**3**) are considered to be biosynthesized by oxidative coupling of two molucules of **1**, we attempted biomimetic synthesis of **2** and **3** from **1**. Treatment of **1** with $FeCl_3$ in acetone at room temperature afforded a mixture of dimeric compounds (yield 32%, 37% of **1** was recovered). HPLC analysis of the mixture showed the presence of **2** and **3** as the major products, which were isolated by preparative HPLC and identified by ^1H-NMR comparison. This result further supported the structures of **2** and **3**.

To our knowledge, rhoipteleic acids A and B are the first example of diastereomeric esters comprising two triterpene and enantiomeric lignan. Furthermore, the presence of these esters of the rare triterpene **1a** in *Rhoiptelea chiliantha* may be important from the point of chemotaxonomical view.

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3. Anderson, G. W.; Callahan, F. M., *J. Am. Chem. Soc.*, **1960**, *82*, 3359 -3363. The ester linkages of **2a** and **3a** could not be cleaved by alkaline treatment.
4. Owing to difficulty of purification, crude sample of **3** contaminated with **2** was used for the methylation and subsequent reactions; hence, the absolute value of the $[\alpha]_D$ of **3** was smaller than that of **2**.

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