Tetranortriterpenoids from *Cipadessa baccifera*

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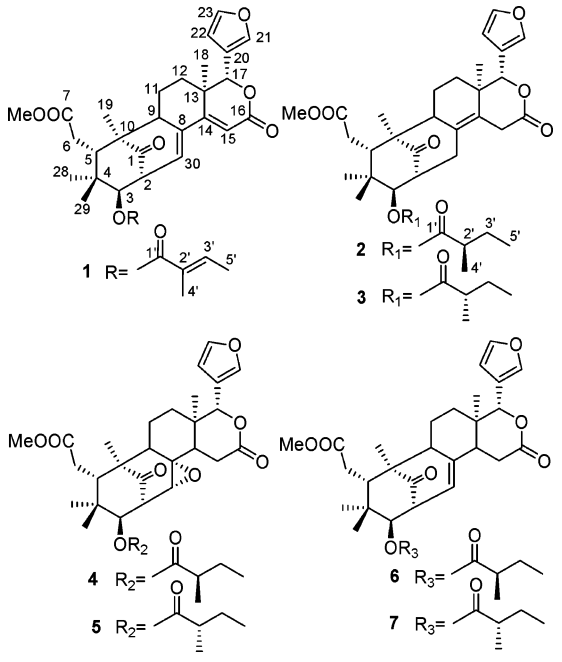
Five new mexicanolide-type tetranortriterpenoids, tigloylseneganolide A (**1**), 2′*R*-methylbutanoylproceranolide (**2**), 2′*S*-methylbutanoylproceranolide (**3**), 2′*R*-cipadesin A (**4**), and 2′*R*-cipadesin (**6**), as well as the known 2′*S*-epimers of **4** and **6** (**5** and **7**), together with six other known limonoids, were isolated from the seeds of *Cipadessa baccifera*. The structures of these compounds were elucidated on the basis of spectroscopic analyses and chemical methods. ^{1}H NMR-based conformational analysis was applied to establish the absolute configuration of the sterically hindered 2-methylbutanoyl in three epimeric pairs (**2**−**7**). A general rule for the determination of the absolute configurations of 2*R*- and 2*S*-methylbutanoyl groups at C-3 of a limonoid in a mixture is proposed.

Limonoids that have antifeedant, antimicrobial, or antimalarial activities, isolated from the plants of the Meliaceae family, are of interest to both phytochemists and agrochemists.[1,2] *Cipadessa baccifera* (Roth.) Miq. (Meliaceae) is a shrub and has been used in folk medicine for the treatment of rheum, dysentery, and pruritus.[3] Previous study on the seeds of *C. baccifera* reported three tetranortriterpenoids and some other compounds.[4] As part of our continuing work on the chemical constituents of plants of the Meliaceae family,[5] five new mexicanolide-type tetranortriterpenoids, tigloylseneganolide A (**1**), 2′*R*-methylbutanoylproceranolide (**2**), 2′*S*-methylbutanoylproceranolide (**3**), 2′*R*-cipadesin A (**4**), and 2′*R*-cipadesin (**6**), as well as the known 2*S*-epimers of **4** and **6** (**5** and **7**), together with six other known limonoids, have been isolated from seeds of *Cipadessa baccifera* that were collected in Xishuangbanna, China.



Results and Discussion

Compound **1**, a white powder, had the molecular formula $C_{32}H_{38}O_8$ as established on the basis of HREIMS at *m*/*z* 550.2569 $[M]^+$ (calcd 550.2567). The IR spectrum showed the presence of carbonyl (1720 cm^{-1}) and double-bond (1649 cm^{-1}) groups. The ^{1}H NMR spectrum (Table 1) had three resonances at δ 7.50 (1H, dd, J = 0.8, 0.7 Hz, H-21), 7.43 (1H, dd, J = 1.6, 1.7 Hz, H-23), and 6.48 (1H, dd, J = 1.7, 0.7 Hz, H-22), typical of a β-substituted furan ring; two olefinic proton resonances at δ 6.25 (1H, dd, J = 6.0, 2.8 Hz) and 6.16 (1H, s), typical of trisubstituted double bonds; proton signals at δ 5.15 (1H, s) and 4.90 (1H, d, J = 9.1 Hz) indicating two oxygenated methines; and resonances at δ 1.20, 1.04, 0.83, and 0.79 for four angular methyl groups. A tigloyl group was also indicated by the proton signals at δ 7.00 (1H, qd, J = 7.0, 1.4 Hz, H-3′), 1.92 (3H, s, H_3-4′), and 1.90 (3H, d, J = 7.4 Hz, H_3-5′). Combined with the ^{13}C NMR spectrum, the NMR data indicated that compound **1** was a mexicanolide-type tetranortriterpenoid with a limonoid core, the same as that of seneganolide A.[6] Comparison of the NMR and MS data of **1** with those of seneganolide A indicated that compound **1** was its 3-*O*-tigloyl derivative. This was confirmed by the HMBC spectrum, in which the tigloyl group was connected to C-3 by the correlation between H-3 and C-1′. The NOESY correlation between H-3 and H-2 indicated that the *O*-tigloyl was β-oriented. The relative configuration of the limonoid core in **1** was further confirmed by the NOESY spectrum. Therefore, compound **1** was identified as tigloylseneganolide A.

Compound **2** showed a HREIMS molecular ion peak at *m*/*z* 554.2872 corresponding to the molecular formula $C_{32}H_{42}O_8$ (calcd 554.2880). The strong and broad IR absorption band at 1732 cm^{-1} revealed the presence of carbonyl groups. The ^{1}H NMR resonances at δ 7.54 (H-21, d, J = 0.7 Hz), 7.40 (H-23, dd, J = 1.8, 1.5 Hz), and 6.47 (H-22, d, J = 1.2 Hz) were typical for a β-furan, and the resonances at δ 1.14 (s), 1.05 (s), 0.81 (s), and 0.72 (s) were assignable to four angular methyl groups. These data suggested that compound **2** was likely to be a mexicanolide-type tetranortriterpenoid. The ^{13}C NMR spectrum (with DEPT) confirmed the above deduction and further indicated the presence of one ketone group (δ 218.1), two esters (δ 174.1, C-7; 169.8, C-16), and one double bond (δ 131.7, C-14; δ 127.7, C-8). A 2-methylbutyryloxy group was identified by the proton resonances at δ 1.23 (H_3-4′, d, J = 6.9 Hz) and 0.90 (H_3-5′, t, J = 7.4 Hz) in the ^{1}H NMR and an ester carbonyl at δ 176.3 in the ^{13}C NMR. Detailed analysis of spectroscopic data of **2** suggested that it was probably a 2-methylbutanoyl derivative of proceranolide.[7] The HMBC experiment confirmed the backbone of **2** and located the 2-methylbutanoyl at C-3 by the correlation between H-3 and C-1′. Analysis of the NOESY spectrum of **2**, 2′*R*-methylbutanoylproceranolide, indicated that the relative configuration of the limonoid skeleton was the same as proceranolide.

Compound **3** was isolated along with its 2′*R*-epimer (**2**) by semipreparative HPLC with a reversed-phased C8 silica gel

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Table 1. ^{1}H NMR Data of Compounds **1**−**3** in $CDCl_3$ at 400 MHz.

	1	**2**	**3**
2	3.72 (1H, m)	3.17 (1H, ddd, 9.8, 6.1, 2.0)	3.16 (1H, ddd, 9.8, 6.1, 2.0)
3	4.90 (1H, d, 9.2)	4.95 (1H, d, 10.1)	4.97 (1H, d, 10.0)
5	3.33 (1H, dd, 9.9, 2.2)	3.23 (1H, dd, 9.3, 3.3)	3.24 (1H, dd, 9.3, 3.6)
6	2.37 (2H, m)	2.35 (2H, m)	2.37 (2H, m)
9	2.25 (1H, m)	2.04 (1H, br s)	2.05 (1H, br s)
11	α 1.75 (1H, m)	1.79 (2H, m)	1.79 (2H, m)
	β 1.49 (1H, m)		
12	α 1.27 (1H, m)	α 1.09 (1H, m)	α 1.10 (1H, m)
	β 1.95 (1H, m)	*β* 1.75 (1H, m)	*β* 1.75 (1H, m)
15	6.16 (1H, s)	α 3.45 (1H, dt, 20.9, 2.9)	α 3.44 (1H, dt, 20.6, 2.7)
		β 3.74 (1H, d, 21.1)	*β* 3.77 (1H, d, 20.7)
17	5.15 (1H, s)	5.64 (1H, s)	5.67 (1H, s)
18	1.03 (3H, s)	1.05 (3H, s)	1.06 (3H, s)
19	1.20 (3H, s)	1.14 (3H, s)	1.15 (3H, s)
21	7.50 (1H, dd, 0.8, 0.7)	7.54 (1H, d, 0.7)	7.55 (1H, d, 0.7)
22	6.48 (1H, dd, 1.8, 0.7)	6.47 (1H, d, 1.2)	6.47 (1H, d, 1.2)
23	7.43 (1H, dd, 1.6,1.7)	7.40 (1H, dd, 1.8, 1.5)	7.41 (1H, dd, 1.7, 1.7)
28	0.82 (3H, s)	0.81 (3H, s)	0.81 (3H, s)
29	0.79 (3H, s)	0.72 (3H, s)	0.72 (3H, s)
30	6.25 (1H, dd, 6.0, 2.8)	α 2.12 (1H, dd, 16.1, 5.4)	α 2.13 (1H, br d, 15.2)
		β 2.77 (1H, dd, 14.9, 1.9)	*β* 2.78 (1H, dd, 15.5, 1.9)
OMe	3.69 (3H, s)	3.70 (3H, s)	3.70 (3H, s)
2′		2.46 (1H, m)	2.43 (1H, m)
3′	7.00 (1H, q, 7.0, 1.4)	a 1.70 (1H, m)	a 1.71 (1H, m)
		b 1.51 (1H, m)	b 1.50 (1H, m)
4′	1.92 (3H, t, 1.2)	1.23 (3H, d, 6.9)	1.19 (3H, d, 7.3)
5′	1.90 (3H, dd, 6.9, 1.2)	0.90 (3H, t, 7.4)	1.00 (3H, t, 7.3)

Table 2. ^{1}H NMR Data of Compounds **4**−**7** in $CDCl_3$ at 400 MHz.

	4	**5**	**6** (**7**)
2	3.57 (1H, dd, 9.5, 2.5)	3.56 (1H, dd, 9.5, 2.5)	3.48 (1H, m)
3	5.08 (1H, d, 9.7)	5.08 (1H, d, 9.4)	4.81 (1H, d, 9.5)
5	3.23 (1H, dd, 8.0, 2.8)	3.22 (1H, dd, 7.9, 3.4)	3.41 (1H, m)
6	2.34 (2H, m)	2.34 (2H, m)	2.36 (2H, m)
9	1.92 (1H, m)	1.91 (1H, m)	2.23 (1H, br s)
11	α 1.78 (1H, m)	α 1.78 (1H, m)	a 2.08 (1H, m)
	β 1.84 (1H, m)	*β* 1.83 (1H, m)	b 1.68 (1H, m)
12	α 1.18 (1H, m)	α 1.17 (1H, m)	a 1.66 (1H, m)
	β 1.95 (1H, m)	*β* 1.95 (1H, m)	b 1.46 (1H, m)
14	1.57 (1H, m)	1.55 (1H, m)	2.19 (1H, br s)
15	α 2.79 (1H, dd, 15.8, 4.7)	α 2.79 (1H, dd, 15.7, 4.6)	a 2.89 (1H, dd, 18.7, 6.0)
	β 3.65 (1H, dd, 15.6, 14.7)	*β* 3.66 (1H, dd, 15.4, 15.1)	b 2.81 (1H, br d, 18.8)
17	5.16 (1H, s)	5.15 (1H, s)	5.68 (1H, s)
18	1.00 (3H, s)	1.00 (3H, s)	1.08 (3H, s)
19	1.06 (3H, s)	1.06 (3H, s)	1.14 (3H, s)
21	7.47 (1H, d, 1.0)	7.46 (1H, s)	7.78 (1H, s)
22	6.45 (1H, dd, 1.1, 0.7)	6.44 (1H, d, 1.2)	6.46 (1H, d, 0.7)
23	7.42 (1H, dd, 2.0, 1.5)	7.42 (1H, dd, 1.7, 1.2)	7.41 (1H, s)
28	0.80 (3H, s)	0.80 (3H, s)	0.78 (3H, s)
29	0.79 (3H, s)	0.78 (3H, s)	0.82 (3H, s)
30	3.29 (1H, d, 2.5)	3.31 (1H, d, 2.7)	5.37 (1H, d, 6.3)
OMe	3.72 (3H, s)	3.72 (3H, s)	3.71 (3H, s)
2′	2.59 (1H, m)	2.59 (1H, m)	2.44 (1H, m)
3′	a 1.78 (1H, m)	a 1.78 (1H, m)	a 1.66 (1H, m)
	b 1.55 (1H, m)	b 1.54 (1H, m)	b 1.44 (1H, m)
4′	1.24 (3H, d, 7.0)	1.24 (3H, d, 7.1)	1.143 (3H, d, 5.6)
			1.136 (3H, d, 7.0)[a]
5′	0.94 (3H, t, 7.6)	0.96 (3H, t, 7.4)	0.86 (3H, t, 7.4)
			0.92 (3H, t, 7.5)[a]

[a] Chemical shifts of some protons of **7**, where they are different from those of compound **6**.

column. Its IR, UV, and MS spectra closely matched those of **2**. Both compounds showed high similarity in the ^{1}H NMR and ^{13}C NMR spectra, with the main differences being the chemical shifts of H_3-4′ and H_3-5′, suggesting that they were probably 2′-epimers. The NOESY spectrum showed that **3** shared the same relative configurations as **2**, except for C-2′ (see Supporting Information). Finally, the structure of **3** was confirmed by preparation of **3** via esterification of proceranolide[7] (recently isolated from *Swietenia mahagoni* in our group) with (*S*)-2-methylbutyric acid. Thus, compound **3** was assigned as 2′*S*-methylbutanoylproceranolide.

Compounds **4** and **5** were both obtained by semipreparative HPLC as white powders. The ^{1}H NMR (Table 2) and ^{13}C NMR (Table 3) spectra of both compounds were similar to the formerly isolated compound cipadesin A,[8] in which the stereochemistry at C-2′ was left unassigned. Analyses of the spectral data including MS, IR, and 1D and 2D NMR (see Table 2, Table 3, and Supporting Information) suggested that **4** and **5** were a pair of 2′-epimers of cipadesin A. Comparison of the spectroscopic data of **4** and **5** with those reported for cipadesin A revealed that **5**, with a 2′*S*-configuraton, was identical to cipadesin A on the basis of their very similar NMR data and optical rotations ($[\alpha]^{20}_D$ −114 (**5**); $[\alpha]^{20}_D$

Table 3. ^{13}C NMR Data of Compounds **1**−**7** in $CDCl_3$ at 100 MHz.

	1	2	3	4	5	6 (7)
1	214.4	218.1	218.2	214.2	214.3	217.1
2	49.1	48.1	48.1	48.8	48.8	48.8
3	78.3	78.1	78.0	76.8	76.8	76.9
4	38.9	38.3	38.5	39.2	39.4	38.5 (38.6)[a]
5	40.3	40.9	40.9	42.5	42.5	41.4
6	32.9	33.6	33.5	33.1	33.1	32.9
7	173.7	174.1	174.2	174.2	174.2	174.0
8	136.1	127.7	127.7	60.6	60.6	138.4
9	54.1	52.1	52.1	55.9	55.9	56.7
10	52.0	53.0	52.9	48.2	48.2	49.9
11	21.8	18.8	18.7	19.3	19.3	20.6
12	32.9	29.0	29.0	33.4	33.4	34.4
13	37.5	38.2	38.1	36.4	36.4	36.9
14	160.7	131.7	131.7	45.9	45.9	45.2
15	112.4	33.2	33.4	34.0	34.1	29.7
16	164.9	169.8	169.8	172.0	172.0	169.3
17	79.6	80.7	80.6	78.9	78.8	76.9
18	22.2	17.6	17.7	26.4	26.5	21.8
19	15.6	16.6	17.7	15.9	15.8	15.7
20	120.2	120.7	120.6	120.1	120.1	120.7
21	141.4	141.7	141.7	141.0	140.9	141.9
22	110.2	109.9	109.9	110.3	110.3	109.7
23	143.1	142.8	142.8	143.1	143.1	142.9
28	21.0	20.8	20.7	20.9	20.9	22.5 (22.4)[a]
29	22.5	23.4	23.2	22.6	22.4	20.6
30	129.2	33.0	33.1	63.3	63.5	122.8
OMe	52.0	52.0	52.0	52.3	52.3	52.1
1′	166.8	176.3	176.3	175.7	175.8	176.1 (176.0)[a]
2′	128.2	41.1	41.5	41.2	41.5	40.4 (40.8)[a]
3′	139.3	27.1	26.3	26.9	26.6	26.5 (26.3)[a]
4′	12.2	16.1	16.6	16.7	17.4	15.8 (16.2)[a]
5′	14.7	11.4	11. 7	11.6	11.9	11.3 (11.4)[a]

[a] Chemical shifts of some carbons of **7**, where they are different from those of compound **6**.

−103 reported for cipadesin A). 2′*R*-Cipadesin A (**4**) was thus identified as a new compound.

2′*R*-Cipadesin and 2′*S*-cipadesin (**6** and **7**) were isolated in a mixture by semipreparative HPLC (even under several optimized HPLC conditions). ^1H NMR (Table 2) analysis of the mixture of **6** and **7** showed that they were in a ratio of 3:5 as determined by the values of the integral area on H_3-5′. All the proton resonances of **6** and **7** were overlapped except for those of H_3-4′ and H_3-5′ in the ^1H NMR spectrum. ^1H NMR data showed that compound **7**, with a 2′*S*-configuration, was identical to cipadesin,[5a] as determined by the closely related chemical shifts of H_3-4′ and H_3-5′. 2′*R*-Cipadesin (**6**) was therefore identified as a new compound.

The stereochemistry at C-2′ for the three 2′-epimeric pairs was assigned by detailed ^1H NMR-based conformational analyses (Figure 1). The considerable steric interaction between the 2-methylbutanoyl group and the limonoid core made one stable conformation dominant in solution. Therefore, the ^1H NMR of the compounds with a 2′*R*- (in the cases of **2**, **4**, **6**) and a 2′*S*-methylbutanoyl group at C-3 (in the cases of **3**, **5**, **7**) showed slight differences in the acyl part. On biogenetic considerations, the absolute configurations of the limonoid cores of compounds **1**−**7** are assumed as depicted, and the absolute configurations of C-2′ in the acyls of compounds **2**−**5** could be assigned from NOESY spectra. Therefore, compound **2** was assigned to have a 2′*R*-configuration on the basis of NOESY correlations of H_3-4′, H-2′/H_β-15 and H_3-5′/H_3-29, and compound **3** was assigned as having a 2′*S*-configuration by the ROESY correlations of H_3-4′/H_3-29 and H-2′/H_β-15, which is identical to the result determined by the chemical method. The C-2′ absolute configurations of compounds **4** and **5** were assigned as 2′*R*- and 2′*S*-cipadesin A, respectively, in a similar manner.

Furthermore, on the basis of the ^1H NMR conformational analysis (Tables 1 and 2, Figure 1), a general rule for the determination of the absolute configurations of 2*R*- and 2*S*-methylbutanoyl at the C-3 of a limonoid in a mixture was proposed. CH_3-4′ was more deshielded in the case of 2′*R* than that having a 2′*S*-configuration ($\delta_R - \delta_S$ (CH_3-4′) > 0: $\Delta\delta_{2,3} = \delta_R - \delta_S = +13.9$ Hz; $\Delta\delta_{4,5} = +2.8$ Hz; $\Delta\delta_{6,7} = +2.0$ Hz), and CH_3-5′ was more shielded in the case of 2′*R* than that having a 2′*S*-configuration ($\delta_R - \delta_S$ (CH_3-5′) < 0: $\Delta\delta_{2,3} = \delta_R - \delta_S = -40.3$ Hz; $\Delta\delta_{4,5} = -10.0$ Hz; $\Delta\delta_{6,7} = -21.2$ Hz) (Figure 1). Thus, compounds **6** and **7** in a mixture were assigned as 2′*R*- and 2′*S*-cipadesin, respectively.

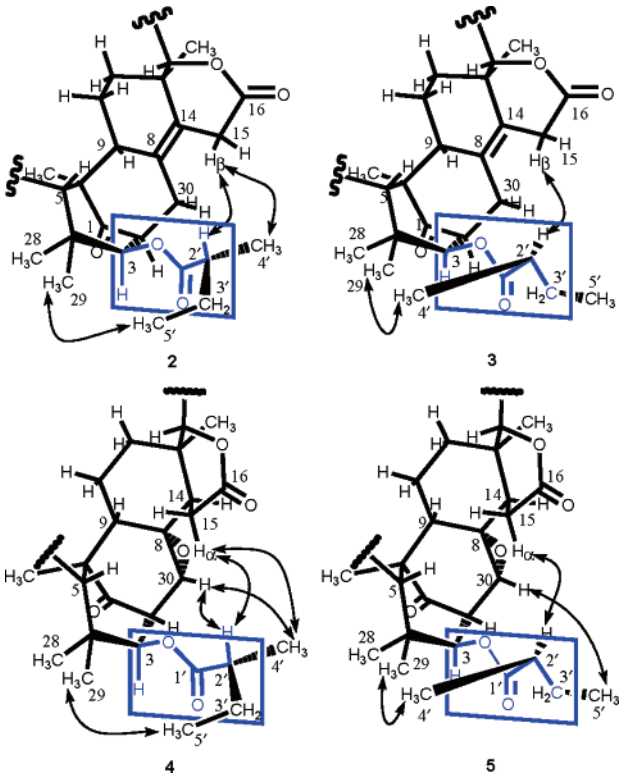

Figure 1. Conformational analysis of the 2′*R* (**2** and **4**) and 2′*S* (**3** and **5**) methylbutanoyls in the compounds **2**−**5**; "↔" represent NOESY correlations.

The six other nortriterpenoids were identified to be ruageanin A[9], swietemahonolide,[10] febrifugin,[11] methyl 3β-isobutyryloxy-1-oxomeliac-8,30-enate,[12] khayasin T,[13] and 3β-isobutyryloxymexicanolide[14] using 1D NMR and MS data.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a Perkin-Elmer 341 polarimeter. UV spectra were measured on a Shimadzu UV-2550 spectrophotometer. IR spectra were recorded on a Perkin-Elmer 577 spectrometer with KBr disks. NMR spectra were measured on a Bruker AM-400, Varian Inova-400, or Varian Inova-600 spectrometer with TMS as internal standard. EIMS (70 eV) and ESIMS were carried out on a Finnigan MAT95 mass spectrometer and a Finnigan LC Q^{DECA} instrument, respectively. All solvents were of analytical grade (Shanghai Chemical Plant, Shanghai, People's Republic of China). Silica gel (200−300 mesh) was used for column chromatography, and precoated silica gel GF254 plates (Qingdao Haiyang Chemical Plant, Qingdao, People's Republic of China) were used for TLC. C_{18} reversed-phased silica gel (150−200 mesh, Merck), MCI gel (CHP20P, 75−150 μm, Mitsubishi Chemical Industries Ltd.), and Sephadex LH-20 gel (Amersham Biosciences) were used for column chromatography. Semipreparative HPLC was performed on a Waters 515 pump equipped with a Waters 2487 detector and a YMC-Pack ODS-A column (250 × 10 mm, S-5 μm, 12 nm).

Plant Material. *C. baccifera* (Roth.) Miq. was collected in Xishuangbanna, Yunnan Province, People's Republic of China, and authenticated by Professor You-Kai Xu of the Xishuangbanna Tropical Botanical Garden (XTBG), Chinese Academy of Sciences. A voucher specimen has been deposited in Shanghai Institute of Materia Medica, Chinese Academy of Sciences (accession number: CBA-2006-2Y).

Extraction and Isolation. Powdered air-dried seeds of *C. baccifera* (4.9 kg) were extracted with 95% EtOH at room temperature to give a crude extract (903 g), which was suspended in 1.5 L of H_2O and extracted with petroleum ether (1000 mL × 3) and EtOAc (1000 mL × 3), respectively. The EtOAc extract (60 g) was subjected to an MCI gel column, eluted with H_2O/EtOH (1:0 to 0:1), to afford five fractions, CBE-1 to CBE-5. Fraction CBE-4 was subjected to a silica gel column eluted with petroleum ether/EtOAc (6:1 to 0:1) to obtain two subfractions, E4a and E4b. E4a was separated by semipreparative HPLC with a mobile phase of 80% acetonitrile in water to give 3β-isobutyryloxymexicanolide (6 mg), khayasin T (50 mg), 2′*R*-methylbutanoylproceranolide (**2**, 25 mg), and 2′*S*-methylbutanoylproceranolide (**3**, 12 mg). E4b was separated into two subfractions by a silica gel column eluted with petroleum ether/$CHCl_3$ (1:1). The first subfraction, E4b1, was purified by semipreparative HPLC with a mobile phase of 75% acetonitrile in water to give tigloylseneganolide A (**1**, 5 mg), febrifugin (10 mg), and a mixture of 2′*R*-cipadesin (**6**) and 2′*S*-cipadesin (**7**) (11 mg) in the ratio of 3:5. The second fraction, E4b2, was separated on a reversed-phased C-18 column eluted with 50% ethanol in water to give ruageanin A (20 mg), methyl 3β-isobutyryloxy-1-oxomeliac-8,30-enate (15 mg), and a mixed crystal, which was further purified by semipreparative HPLC with a mobile phase of 65% acetonitrile in water to yield swietemahonolide (9 mg), 2′*R*-cipadesin A (**4**, 11 mg), and 2′*S*-cipadesin A (**5**, 12 mg).

Tigloylseneganolide A (1): white, amorphous solid; $[\alpha]^{20}_D$ +268 (*c* 0.05, MeOH); UV (MeOH) λ_{max} (log ϵ) 211 (4.67), 282 (4.31) nm; IR (KBr) ν_{max} 3431, 2935, 1720, 1649, 1382, 1257, 1153, 1028, 873 cm^{-1}; ^1H NMR, Table 1; ^{13}C NMR, Table 3; EIMS *m*/*z* 550 $[M]^+$ (20), 397 (18), 83 (100), 55 (30); HREIMS *m*/*z* 550.2569 (calcd for $C_{32}H_{38}O_8$, 550.2567).

2′*R*-Methylbutanoylproceranolide (2): white, amorphous solid; $[\alpha]^{20}_D$ −66 (*c* 0.09, MeOH); UV (MeOH) λ_{max} (log ϵ) 200 (3.95), 281 (3.01) nm; IR (KBr) ν_{max} 3435, 2970, 2937, 1732, 1460, 1382, 1256, 1176, 1146, 1026 cm^{-1}; ^1H NMR, Table 1; ^{13}C NMR, Table 3; EIMS *m*/*z* 554 (12) $[M]^+$, 458 (48), 430 (100), 328 (25), 210 (24), 85 (36), 57 (66); HREIMS *m*/*z* 554.2872 (calcd for $C_{32}H_{42}O_8$, 554.2880).

2′*S*-Methylbutanoylproceranolide (3): white, amorphous solid; $[\alpha]^{20}_D$ −85 (*c* 0.06, MeOH); UV (MeOH) λ_{max} (log ϵ) 200 (4.20), 281 (3.37) nm; IR (KBr) ν_{max} 3439, 2928, 2852, 1732, 1462, 1381, 1257, 1178, 1147, 1026 cm^{-1}; ^1H NMR, Table 1; ^{13}C NMR, Table 3; EIMS *m*/*z* 554 (12) $[M]^+$, 458 (48), 430 (96), 328 (28), 210 (28), 85 (50), 57 (100).

Preparation of 3 from (*S*)-2-Methylbutyric Acid and Proceranolide. To a solution of CH_2Cl_2 (3 mL) containing 5 mg of oxalyl chloride and a catalytic amount of DMF was added 5 mg of (*S*)-2-methylbutyric acid, and the mixture was stirred at room temperature. Then, 3 mg of proceranolide in 3 mL of CH_2Cl_2 was added dropwise. The reaction mixture was stirred for 2 h at room temperature. After workup, the resulting product was purified by semipreparative HPLC to give compound **3a.** Co-injection of **3a** with **2**, or **3a** with **3**, on HPLC (80% acetonitrile in water) and MS showed that **3a** was identical to **3**.

2′*R*-Cipadesin A (4): white, amorphous solid; $[\alpha]^{20}_D$ −145 (*c* 0.08, MeOH); UV (MeOH) λ_{max} (log ϵ) 200 (3.93), 206 (3.93) nm; IR (KBr) ν_{max} 3435, 2972, 1732, 1460, 1382, 1261, 1180, 1146, 1026 cm^{-1}; EIMS *m*/*z* 570 (38) $[M]^+$, 432 (20), 323 (40), 221 (100), 57 (48); HREIMS *m*/*z* 570.2832 (calcd for $C_{32}H_{42}O_9$, 570.2829).

2′*S*-Cipadesin A (5): white, amorphous solid; $[\alpha]^{20}_D$ −114 (*c* 0.07, MeOH); UV (MeOH) λ_{max} (log ϵ) 200 (3.94), 206 (3.89) nm; IR (KBr) ν_{max} 3437, 2974, 1736, 1458, 1263, 1186, 1148, 1024 cm^{-1}; EIMS *m*/*z* 570 (28) $[M]^+$, 432 (18), 323 (40), 221 (100), 57 (50).

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Supporting Information Available: ^1H NMR spectra of the three epimeric pairs **2**−**7**; HMBC spectra of compounds **1**, **2**, and **5**; NOESY spectra of compunds **1**, **2**, **4**, and **5**; ROESY spectra of **3**; enlarged ^1H NMR spectrum (δ 0.7−1.3 ppm) of **6** and **7** in a mixture. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

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