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TWO NEW XANTHYLETIN-TYPE COUMARINS FROM *PEUCEDANUM DECURSIVUM*

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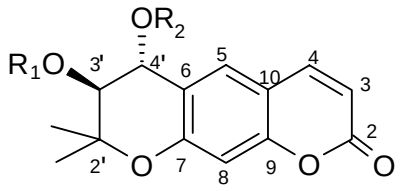
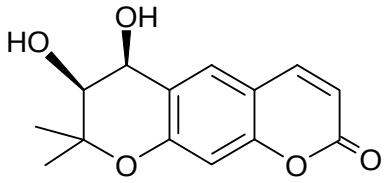
Abstract—Two new xanthyletin-type coumarins were isolated from the root of *Peucedanum decursivum* and the structures were established as 3′(*S*), 4′(*R*)-biangeloyloxys-3′,4′-dihydroxanthyletinand3′(*S*)-senecioyloxy-4′(*R*)-angeloyloxy-3′,4′-dihydroxanthyletin, respectively, by spectroscopic methods. The absolute configurations were deduced by chemical correlations with known compounds.

The root of *Peucedanum decursivum* (Miq.) Maxim and *P. praeruptorum* Dunn is a traditional Chinese medicine widely used for the treatment of such diseases as cough due to pathogenic wind - heat, accumulation of phlegm and heat in the lung. The former contains xanthyletin-type coumarins,[1] and the latter seselin-type coumarins.[2] This paper describes the isolation and structural elucidation of two new xanthyletin-type coumarins (**1** and **2**) from therootof*Peucedanumdecursivum.*Thestructureswere elucidatedas3′(*S*),4′(*R*)-biangeloyloxys-3′,4′-dihydroxanthyletin(**1**)and3′(*S*)-senecioyloxy-4′(*R*)-angeloyloxy-3′,4′-dihydroxanthyletin (**2**) by spectral analysis, and the absolute configurations were deduced by chemical correlations with known compounds.

Structure of 1 Compound (**1**) was isolated as colorless glassy substance, $[\alpha]_D$ - 53.4° ($CHCl_3$). The molecular ion at *m/z* 426.1654 in the HREI-MS spectrum showed the molecular formula to be $C_{24}H_{26}O_7$.



1. R_1=angeloyl R_2=angeloyl
2. R_1=senecioyl R_2=angeloyl
3. R_1=H R_2=H
5. R_1=senecioyl R_2=senecioyl



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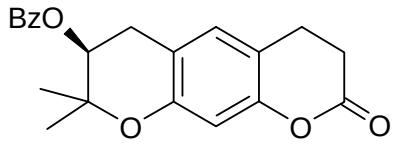

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Figure 1 Structures of **1** ~ **6**

The UV spectrum showed absorption at 221 and 323 nm. The IR absorption bands at 1727, 1629 and 1570 cm^{-1} are attributed to carbonyl group and aromatic moiety of coumarin skeleton, respectively. The ^1H NMR spectrum in the aromatic proton region of **1** contained a pair of doublets at δ 6.25 (1H, d, *J*=9.5 Hz), 7.59 (1H, d, *J*=9.5 Hz) and two singles at δ 7.39 (1H, s), 6.81 (1H, s), which were attributed to C_3 - H, C_4 - H of the α- pyrone ring moiety and C_5 - H, C_8 - H of the benzene ring. These spectral evidence indicated that **1** was a kind of coumarin substituted at C - 6 and C - 7 positions. The doublets at δ 5.37 (1H, d, *J*=6.0 Hz) and 6.16 (1H, d, *J*=6.0 Hz) were assigned to the methine protons at $C_{3'}$ and $C_{4'}$

Table 1. ^1H NMR data of decursitin A (**1**), decursitin B (**2**) and the related compounds

	H-3	H-4	H-5	H-8	H-3′	H-4′	gem-$(CH_3)_2$	CH=C$(CH_3)_2$	CH_3C=CHCH_3
1	6.25	7.59	7.39	6.81	5.37	6.16	1.41		6.18(1H, m) 6.12(1H, m)
	J=9.5				*J*=6.0		1.48		2.03(3H, d, *J*=6.8 Hz) 1.93(3H, d, *J*=6.6 Hz)
2	6.25	7.60	7.42	6.82	5.30	6.11	1.40	5.69(1H, br s)	1.88(6H, s) 6.17(1H, m)
	J=9.5				*J*=5.7		1.47	1.89(3H, s) 2.16(3H, s)	1.87(3H, s) 2.08(3H, d, *J*=6.8 Hz)
Decursidin (**5**)	6.20	7.61	7.38	6.75	5.25	6.03	1.36	5.67(2H, br s) 1.85(6H, s)	
	J=9.5				*J*=6.0		1.43	2.10(3H, s) 2.16(3H, s)	
3	6.40	8.05	7.88	6.88	3.72	4.73	1.43		
	J=9.5				*J*=8.5		1.67		
4	6.23	8.01	7.73	6.67	3.63	4.73	1.25		
	J=9.5				*J*=3.5		1.40		

positions by comparison with the chemical shifts and the coupling pattern of decursidin (**5**) [3] (see Table

1). It showed that **1** was a xanthylethin-type coumarin. The characteristic signals at δ 6.18 (1H, m), 6.12 (1H, m), 2.03 (3H, d, *J*=6.8 Hz), 1.93 (3H, d, *J*=6.6 Hz) and 1.88 (6H, s) showed the existence of two groups of –CO(Me)C=CHMe. No NOE enhancements between δ 2.03 and δ 1.88 as well as δ 1.93 and δ 1.88 was observed in NOE difference spectra, which indicated two angeloyloxys attached to C_{3}' and C_{4}' positions. The structure of **1**, 3′, 4′-biangeloyloxys-3′, 4′-dihydroxanthyletin, was further supported by the ^{13}C NMR spectrum (see Table 2 and Table 3).

Table 2. ^{13}C NMR data of the skeletons of decursitin A (**1**), decursitin B (**2**) and the related compounds

NO	**1**	**2**	Decursidin	**3**	**4**
C-2	160.8	160.8	160.7	163.5	161.4
C-3	113.8	113.8	113.6	113.7	113.1
C-4	143.1	143.2	143.1	146.0	144.4
C-5	129.0	129.0	129.2	129.7	129.0
C-6	117.1	117.0	117.1	124.5	123.8
C-7	156.2	156.2	156.2	157.9	156.5
C-8	104.9	104.9	104.7	104.8	103.6
C-9	155.4	155.4	155.2	156.4	154.9
C-10	113.3	113.3	113.2	114.5	112.7
C-2′	77.9	77.8	77.9	81.7	81.0
C-3′	72.0	71.2	71.2	76.6	75.4
C-4′	66.7	66.7	66.1	69.6	68.5
C-2′-CH_3	22.5	22.7	20.4	20.0	20.0
	25.2	25.0	24.9	27.3	27.3

Table 3. ^{13}C-NMR data of acyl groups of decursitin A (**1**) and decursitin B (**2**)

No.	**1**	**2**
C-1"	166.3	164.9
C-2"	126.9	115.0
C-3"	139.9	159.5
C-4"	15.8	20.5
C-5"	20.5	27.5
C-1"'	167.3	167.3
C-2"'	126.9	127.0
C-3"'	140.6	140.4
C-4"'	16.0	16.0
C-5"'	20.6	20.6

Structure of 2 Compound (**2**) was isolated as colorless glassy substance. $[\alpha]_D$ - 58.4° ($CHCl_3$). The molecular ion at *m/z* 426.1676 in the HREI-MS spectrum showed the molecular formula to be $C_{24}H_{26}O_7$.**2** showed similar UV, IR, ^1H and ^{13}C NMR spectral data to those of **1** (see Tables 1 and 2), the slight differences were only in an angeloyloxy group at δ 2.08 (3H, d, *J*=6.8 Hz), 1.87 (3H, s) and 6.17 (1H, m) whose double bond was *trans*- configuration from the evidence that no NOE enhancements between δ

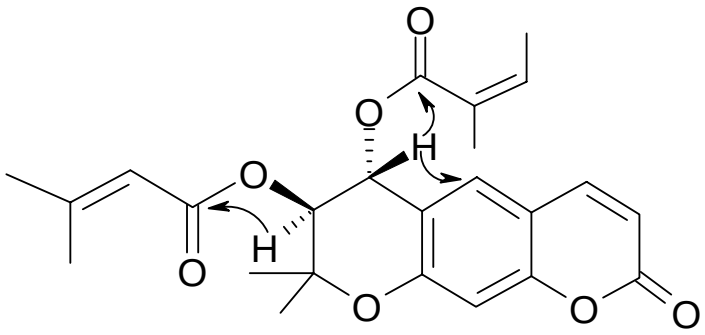
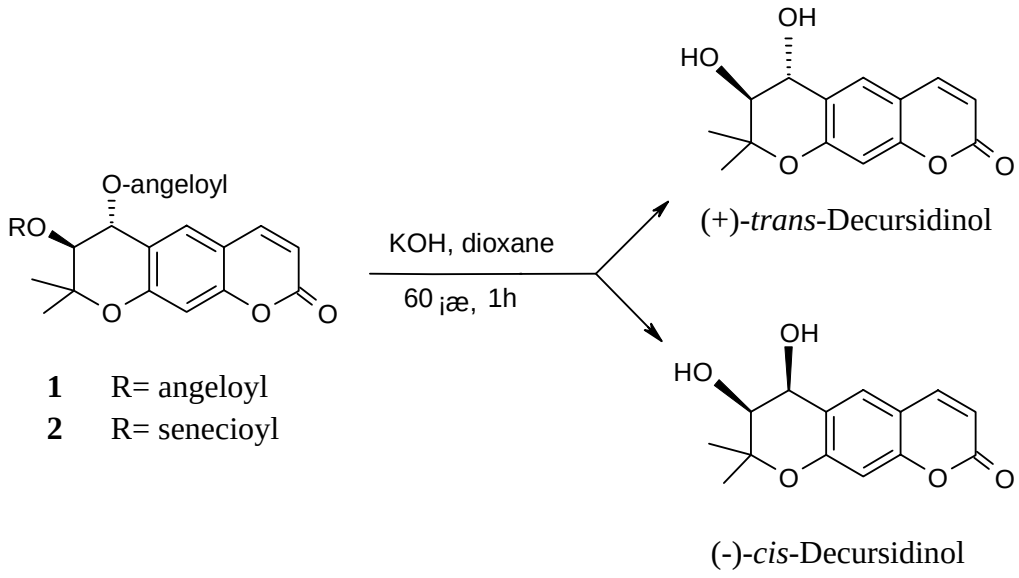


Figure 2 Major correlations in HMBC spectrum of **2**

2.08 and δ 1.87 was observed in NOE difference spectra, and a senecioyloxy group at δ 2.16 (3H, s), 1.89 (3H, s) and 5.69 (1H, br s). The HMBC spectrum showed that the methine proton at δ 5.30 (H-3') correlated with δ 164.9 (senecioyloxy carbonyl) and the methine proton at δ 6.11 (H-4′) correlated with δ 167.2 (angeloyloxy carbonyl) (Figure 2). These 2D NMR evidence suggested that senecioyloxy attached to 3′- position and angeloyloxy to 4′- position. By the above spectroscopic study, **2** was formulated as 3′-senecioyloxy-4′-angeloyloxy-3′,4′-dihydroxanthyletin.

Stereochemistries of skeletons of 1 and 2 The molecular structures of **1** and **2** both contained two chiral carbon atoms. Their relative configurations were determined from the ^{1}H NMR spectrum. According to Sano *et al.* ,[4] 3′, 4′ - *trans* configuration of linear dihydropyranocoumarin derivatives



1 R= angeloyl
2 R= senecioyl

Figure 3 Alkaline hydrolysis of **1** and **2**

gives a larger coupling constant ($J_{3',4'}$ = 5.0 - 9.0 Hz) than that of the corresponding *cis* isomers ($J_{3',4'}$ = 4.0 - 4.2 Hz). The coupling constants of methine protons of compounds (**1**) and (**2**) were 6.0 and 5.7 Hz, respectively. Thus, the 3′, 4′- *trans* configuration was attributed to them. On alkaline hydrolysis, compounds (**1**) and (**2**) gave a mixture containing two products, which were separated by HPLC and identifiedas(+)-*trans*-decursidinol(**3**)whoseC-4′configurationremainedunchanged[1]and(-)-*cis*-decursidinol (**4**) whose C-4′configuration changed [1] by spectral analysis and optical activity (Figure 3). The absolute configurations of **3** and **4** were described previously as 3′(*S*), 4′(*R*) and 3′(*S*), 4′(*S*) by chemical correlations with known compounds, 3, 4-dihydrodecursinol benzoate (**6**) whose absolute configuration was determined by CD spectrum analysis. [4] Therefore, the chemical structures of **1** and **2** were both finally elucidated as 3′(*S*), 4′(*R*)-biangeloyloxys-3′,4′-dihydroxanthyletin and 3′(*S*)-senecioyloxy-4′(*R*)-angeloyloxy-3′, 4′-dihydroxanthyletin, respectively. The absolute configurations of **1** and **2** are identical with decursidin (**5**) which has been isolated from the titled plant in the literature. [3,5]

EXPERIMENTAL

Mps were determined on a X4 micromelting point apparatus. The thermometer was uncorrected. Optical rotations were measured on a PE - 241 MC polarimeter. UV spectra were recorded on a UV - 2051 spectrophotometer in MeOH. IR spectra were recorded on an Impact-410 (Nicolet) spectrophotometer. The 1D NMR and 2D NMR spectra were recorded on Bruker DRX 300 and 400 MHz spectrometers, using TMS as an internal standard. EIMS were measured on JMS - D300 Mass spectrometer. Preparative HPLC was carried out on a Shimadzu Liquid Chromatograph LC-8A equipped with an UV detector using Shim - pack PREP - SIL 20.0 mmID × 25 cm P/N 228 - 00814 - 91 column.

Isolation Roots of *P. decursivum* (Miq.) Maxim were collected in the Laoshan Mountain, Jiangsu Province, China, in November 1996, and identified by Dr. Zhu-Nan Gong, a voucher specimen has been deposited in Department of Natural Medicinal Chemistry, China Pharmaceutical University.

The root material (1.0 kg) was extracted with $CHCl_3$ (3 × 2500 mL) at 50°C for 3 × 3 h. The concentrated extract (76 g) was subjected to silica gel CC (500 g) and eluted by petroleum - EtOAc mixtures gradually in creasing polarity to yield fraction I (petroleum:EtOAc 95:5) (9 g), fraction II (petroleum:EtOAc 90:10) (12 g), fraction III (petroleum:EtOAc 85:15) (18 g) and fraction IV (petroleum:EtOAc 80:20) (15 g) . The fraction II (2 g) was further separated by HPLC (2% EtOAc in cyclohexane, 35 mL/min, UV detector 320 nm) to give compounds (**1**) (352 mg) and (**2**) (264 mg).

Characterization

*3 ´(S),4 ´(R)-biangeloyloxys-3 ´,4 ´-dihydroxanthyletin (**1**)*: A colorless glassy substance. $[\alpha]_D$ = -53.4° ($CHCl_3$, c= 1.5). HREI-MS: *m/z* found 426.1654, calcd 426.1631 for $C_{24}H_{26}O_7$. EIMS *m/z* (ret. int.): 426 M^+ (0.6), 327 (1.5), 326 (4.3), 229 (2.4), 228 (0.5), 227 (1.6), 213 (2.1),185 (0.7), 83 (100), 55 (42.7). UV (MeOH), λ 323 nm (log ε 4.28), 221 (3.87). IR $\nu_{max}cm^{-1}$: 1727, 1629, 1570, 1499, 1457, 1390, 1293, 1248, 1229, 1136, 1050, 983, 938, 852, 826. ^{1}H NMR (300 MHz, $CDCl_3$) see Table 1. ^{13}C NMR (100 MHz, $CDCl_3$) see Table 2 and Table 3.

*3 ´(S)-senecioyloxy-4 ´(R)-angeloyloxy-3 ´,4 ´-dihydroxanthyletin (**2**)*: A colorless glass substance. $[\alpha]_D$ = -58.4° ($CHCl_3$, c= 1.0). HREI-MS: *m/z* found 426.1676, calcd 426.1675 for $C_{24}H_{26}O_7$. EIMS *m/z* (ret. int.): 426 M^+ (0.6), 327 (1.5), 326 (8.0), 312 (1.6), 311 (7.3), 229 (5.2), 227 (1.5), 213 (2.2), 185 (1.1), 149 (31.8), 83 (100), 71 (7.5), 67 (5.2), 57 (25), 55 (31.6). UV (MeOH), λ 325 nm (log ε 4.06), 227 (3.74). IR $\nu_{max}cm^{-1}$: 1734, 1626, 1566, 1457, 1383, 1226, 1136, 1087, 1035. ^{1}H NMR (300 MHz, $CDCl_3$) see Table 1. ^{13}C NMR (100 MHz, $CDCl_3$) see Table 2 and Table 3.

Reaction

*Alkaline hydrolysis of **1*** **1** (150 mg) was dissolved in dioxane (8 mL) containing 0.5 N KOH (3 mL), and heated at 60 °C for 1 h. The reaction mixture acidified with 10% H_2SO_4, was extracted with $CHCl_3$ after standing for 30 min. The $CHCl_3$ solution was washed with saturated $NaHCO_3$, and dried with Na_2SO_4 and evaporated. The residue was subjected to HPLC (100% EtOAc in cyclohexane, 10 mL/min, UV detector 320 nm) to yield (+)-*trans*-decursidinol (**3**) (42 mg) and (-)-*cis*-decursidinol (**4**) (31 mg).

*Alkaline hydrolysis of **2*** **2** (40 mg) was dissolved in dioxane (3 mL) containing 0.5 N KOH (1 mL), and treated as above to yield (+)-*trans*-decursidinol (**3**) (13 mg) and (-)-*cis*-decursidinol (**4**) (9 mg).

*(+)-trans-Decursidinol (**3**)*: Colorless needles, mp :226-228 °C (cyclohexane-EtOAc) (lit., [4] 229-231°C), $[\alpha]_D$ = +115.4° (DMSO, c=0.50) (lit., [4] +144.2°). ^{1}H NMR (300 MHz, CD_3OD) see Table 1. ^{13}C NMR (100 MHz, CD_3OD) see Table 2.

*(-)-cis-Decursidinol (**4**)*: Colorless needles, mp :224-226 °C(cyclohexane-EtOAc) (lit., [4] 226-228°C), $[\alpha]_D$ = -33.4° (DMSO, c=0.22) (lit., [4] –43.8°). ^{1}H NMR (400 MHz, DMSO–d_6) see Table 1. ^{13}C NMR (100 MHz, DMSO–d_6) see Table 2.

ACKNOWLEDGMENT

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