Morinols A and B, Two Novel Tetrahydropyran Sesquineolignans with a New Carbon Skeleton from *Morina chinensis*

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Two sesquineolignans, each bearing a tetrahydropyran ring with a new carbon skeleton and named morinols A and B, have been isolated from the roots of a Chinese medicinal herb, *Morina chinensis*. Their structures have been determined on the basis of spectroscopic evidences, as well as a simple chemical transformation.

As a Chinese traditional medicinal plant, *Morina chinensis* (Dipsacaceae) has been used for the treatment of many diseases since ancient times,[1] and has also been used as Tibetan medicine. It is mainly distributed in northwestern China. In this communication, we wish to report two novel tetrahydropyran sesquineolignans with a new carbon skeleton, named morinols A (**1**) and B (**2**), from this Chinese traditional herb.

Lignans and neolignans have attracted much interest over the years, both on account of their widespread occurrence in nature and their broad range of biological activities. In 1976, Ichihara *et al.*[2] reported two novel lignans which were isolated from the roots of *Arctium lappa L.*, and on the basis of the definitions of lignan and neolignan, they proposed the term of sesquilignan for the first time. Morinols A (**1**) and B (**2**) were typical sesquineolignan compounds, each bearing a tetrahydropyran ring in its structure. There is no previous report on this kind of lignans, both of the two compounds having a new carbon skeleton.

Morina chinensis was collected in the south of Qinghai province, China. The $CHCl_3$ soluble portion (120 g) of the MeOH extract of the roots (1.8 kg) of this plant was chromatographed over a silica gel column and eluted with *n*-hexane-acetone, where thirteen fractions were obtained. Fraction 12 (*n*-hexane-acetone; 1:1) was separated by using repeated silica gel column chromatography, and then purified by GPC (Shodex H-2001, 2002, $CHCl_3$) and HPLC (Si 60, Hibar RT 250-25), affording morinols A (**1**) (52 mg) and B (**2**) (37 mg).

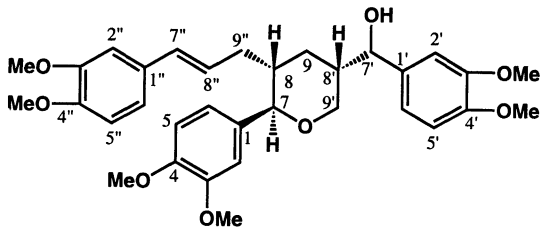

Figure 1. Structure of compound **1** (morinol A).

Morinol A (**1**)[3] was obtained as a colourless oil. The positive HRFABMS (565.2793, calcd. for $C_{33}H_{41}O_8$, 565.2801) showed the molecular formula to be $C_{33}H_{40}O_8$, which was supported by ^1H and ^{13}C NMR spectral data (Table 1), so its unsaturation value was 14. ^{13}C NMR and DEPT spectral data of **1** displayed the presence of three aromatic rings (DEPT indicated nine carbons of the aromatic rings were quaternary), a double bond, six methoxyl groups, three methylenes (δ 33.2, C-9; δ 71.0, C-9′; δ 35.8, C-9″) among which one of them (δ 71.0, C-9′) should be connected with oxygen, and four methines (δ 85.5, C-7, 41.9, C-8; δ 77.1, C-7′, 43.5, C-8′) while two of them (δ 85.5, C-7; δ 77.1, C-7′) should be connected with oxygen. That is to say, there were three aromatic rings and nine other carbons except the six methoxyl groups in compound **1**, just like three C_6-C_3 units. Furthermore, there must be another ring in the structure of **1**, because the unsaturation values of the three aromatic rings and the double bond sum up to only 13.

In the ^1H-^1H COSY spectrum of **1**, the correlations of H-7′ to H-8′, H-8′ to H-9′ and H-9, H-9 to H-8, H-8 to H-7 and H-9″, H-9″ to H-8″, H-8″ to H-7″, suggested the structure as shown. The chemical shift of H-7′ of the acetate of compound **1** showed significant downfield shift (from δ_H 4.39 to 5.49), verifying a hydroxy group must be on C-7′. Then, C-7 and C-9′ should be linked by an oxygen atom according to both the given molecular formula of compound **1** and the chemical shifts of C-7 and C-9′. In the HMBC spectrum of **1**, the correlations of H-7 with C-1, C-2, C-6, C-9, C-9″ and C-9′; either of H_2-9 with C-9″, C-7, C-7′ and C-9′; H-7′ with C-1′, C-2′, C-6′, C-9′ and C-9; H-7″ with C-1″, C-2″, C-6″, C-8″ and C-9″, further confirmed the structure.

The signal of H-7 in **1** was overlapped with the signals of the methoxy groups when $CDCl_3$ was used as solvent, but they were separated just as expected when CD_3OD was used as solvent, and showed that the coupling constant between H-7 and H-8 was J = 9.6 Hz. Thus, H-7 and H-8 were in *trans* relationship. H-8′ should adopt an *axial* orientation according to both the splitting pattern and the coupling constants to H-9′α and H-9′β. These relative configurations were confirmed by the correlations of H-9β with H-8, H-8′ and H-9′β; H-9′α with H-7 and H-7′ in the NOESY spectrum. Hence, the structure of compound **1** has been determined as shown (Figure 1), named as morinol A.

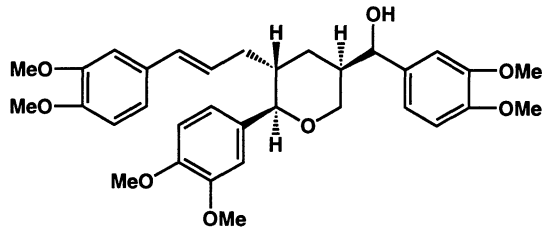

Figure 2. Structure of compound **2** (morinol B).

Morinol B (**2**)[4] was obtained as a colourless oil. Its NMR spectral data (Table 1) were very similar to those of compound **1**. The chemical shift of H-7′ of the acetate of compound **2** also showed significant downfield shift (from δ_H 5.07 to 6.10). The positive HRFABMS (565.2801, calcd. for $C_{33}H_{41}O_8$, 565.2801) of **2** gave the molecular formula of $C_{33}H_{40}O_8$, the same as that of

Table 1. NMR spectral data of compounds **1** and **2** ($CDCl_3$ as solvents; 400 MHz for ^{1}HNMR, 100 MHz for ^{13}CNMR; δ, ppm)

	Compound **1**		Compound **2**	
No.	C	H	C	H
1	133.6 s		133.6 s	
2	109.3 d	6.92, d (1.4)	109.0 d	6.95, d (1.4)
3	[b]149.1 s		[b]148.9 s	
4	[b]149.2 s		[b]149.0 s	
5	111.1 d	6.78, d (8.4)	111.1 d	6.77, d (8.4)
6	118.8 d	6.84, dd (8.4, 1.4)	118.9 d	6.87, dd (8.4, 1.4)
7	85.5 d	overlapped by OMe	85.9 d	4.00, d (9.7)
8	41.9 d	1.77, m	38.4 d	1.98, m
9	33.2 t	1.13, q (12.0)	31.9 t	1.44, ddd (13.0, 13.0, 5.0)
		1.70, br d (12.0)		1.68, br d (13.0)
1′	135.5 s		136.4 s	
2′	110.3 d	6.89, d (1.4)	110.7 d	6.72, d (1.3)
3′	[b]148.8 s		[b]149.1 s	
4′	[b]149.0 s		[b]149.3 s	
5′	110.9 d	6.73, d (8.5)	111.2 d	6.75, d (8.5)
6′	120.3 d	6.88, dd (8.5, 1.4)	120.0 d	6.96, dd (8.5, 1.3)
7′	77.1 d	4.39, d (9.1)	74.0 d	5.07, d (9.0)
8′	43.5 d	2.17, m	41.7 d	1.92, m
9′	71.0 t	4.38, br d (11.2)	68.7 t	4.50, d (11.7)
		3.42, t (11.2)		3.74, dd (11.7, 2.6)
1″	130.7 s		130.7 s	
2″	108.5 d	6.91, d (1.3)	108.6 d	6.95, d (1.4)
3″	[b]148.4 s		[b]148.4 s	
4″	[b]148.7 s		[b]148.6 s	
5″	110.9 d	6.76, d (8.5)	110.7 d	6.78, d (8.5)
6″	118.8 d	6.87, dd (8.5, 1.3)	118.8 d	6.89, dd (8.5, 1.4)
7″	131.2 d	6.09, d (15.6)	131.2 d	6.08, d (15.7)
8″	125.7 d	5.71, dt (15.6, 7.4)	125.5 d	5.69, dt (15.7, 7.5)
9″	35.8 t	1.80, m; 1.98, m	35.7 t	1.75, m; 1.97, m
OMe	55.8,	3.86 X 3, 3.87,	55.8 X 2	3.85, 3.86, 3.87 X 2,
	55.9 X 2	3.88 X 2	55.9 X 2	3.88, 3.89
	56.0 X 3		56.0, 56.1	

[a]Figures in parentheses are coupling constants in Hz.
[b]Assignments in the same column may be interchanged.

1. The evident differences between compounds **1** and **2** were the chemical shifts of H-7′, C-7′, H-9′ and C-9′, especially the splitting pattern and the coupling constants of H-9 and H-9′.

In compound **2**, H-8′ should adopt an *equatorial* orientation by comparison of the splitting pattern and the coupling constants to H-9′α, H-9′β, H-9α and H-9β with those of **1**. In the NOESY spectrum of **2**, the correlations of H-9β with H-8, H-7′ and H-9′β; H-7′ with H-9′β and H–8; H-9′α with H-7, H-8′ and H-9α, further confirmed the relative configuration. Thus, compound **2** (Figure 2) was a configurational isomer of compound **1**, named as morinol B. All of the spectral data were assigned on the basis of the correlations of ^{1}H-^{1}H COSY, HSQC and HMBC.

The H-7′ and H-8′ should be *anti* for both compounds **1** and **2**, due to their coupling constants were $J_{7',8'}$ = 9.1 Hz and 9.0 Hz, respectively, but the relative configurations at this bond are not reliably determined according to NOE or the molecular model study.

In order to determine the absolute configuration at C-7′, the (R)- and (S)-MTPA esters of compound **2** were obtained using modified Mosher's method. However, the ^{1}H NMR spectra of both (R)- and (S)-MTPA esters showed the separated pairs of signals, while these separated signals are with the same chemical shifts in **2**. This results indicated compound **2** should be an enatiomer mixture, and the ratio of two enatiomer isomers is about 1:1 according to the integral of the separated signals. The structure of **1** is very similar to that of **2**, furthermore, the optical rotation values for both **1** and **2** are near zero. Thus, we speculate **1** is also an enantiomeric natural product.

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References and Notes

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2 A. Ichihara, K. Oda, Y. Numata, and S. Sakamura, *Tetrahedron Lett.*, **44**, 3961 (1976).

3 $[\alpha]_D^{25}$ = +0.98^0 (c=1.016; $CHCl_3$); IR (KBr) ν_{max} cm^{-1}: 3856, 3478, 3435, 2362, 2343, 1656, 1639, 1511, 1265, 1140, 1028, 670; UV ($CHCl_3$) λ_{max} nm (log ε): 272.5 (3.94), 240.2 (3.93).

4 $[\alpha]_D^{25}$ = -3.92^0 (c=0.510; $CHCl_3$); IR (KBr) ν_{max} cm^{-1}: 3856, 3652, 3632, 3478, 3436, 2364, 2346, 1655, 1639, 1510, 1460, 1264, 1140, 1028, 570; UV ($CHCl_3$) λ_{max} nm (log ε): 272.5 (3.95), 241.4 (3.89).