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# Morinols A-L, Twelve Novel Sesquineolignans and Neolignans With a New Carbon Skeleton from *Morina chinensis*

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***Abstract:*** Two novel tetrahydropyran sesquineolignans with a new carbon skeleton, named morinols A (**1**) and B (**2**), and other ten novel neolignans, named morinols C-L (**3-12**), along with two known lignans, pinoresinol (**13**) and lariciresinol (**14**), have been isolated from the roots of Chinese medicinal herb, *Morina chinensis*. The structures of all of the compounds have been determined mainly on the basis of modern spectroscopic evidences ($^1$H NMR, $^{13}$C NMR, DEPT, $^1$H-$^1$H COSY, NOESY, HSQC, HMBC and HRMS), as well as chemical transformation. The inhibitory effects of the isomers, morinols A (**1**) and B (**2**), on cytokine production have been studied, the results indicated that morinol B (**2**) has more stronger activity than morinol A (**1**). Morinols B (**2**), E (**5**) and G (**7**) were verified should be enantiomeric natural products by means of MTPA and 2NMA.


***Keywords:*** *Morina chinensis;* Dipsacaceae; neolignans; sesquineolignans; new carbon skeleton; cytokine production; morinols A-L; enantiomeric natural product.

## INTRODUCTION

As a very important class of natural products, lignans and neolignans have been attracted much interest over the years, both on account of their widespread occurrence in nature and a lot of bioactivities, such as contraceptive,[1] antitumor,[2] antivitral,[3] and cytotoxic[4] activities. The term of lignan was introduced by Haworth[5,6] around 1940 for a category of natural products having a common constitutional feature of two $C_6$-$C_3$ (*n*-propylbenzene) residues linked by a bond connecting the central (β) carbon atoms of each side-chain. In 1969, McCredie *et al.*[7] proposed that the definition of lignans should be extended to cover all natural products of low molecular weight that arise primarily from the oxidative coupling of *p*-hydroxyphenylpropane units. The term of neolignan was introduced by Gottlieb[8] to designate compounds in which the two $C_6$-$C_3$ units are not linked by a β-β′ bond. In 1976, Ichihara *et al.*[9] reported two novel lignans which isolated from the roots of *Arctium lappa* L., on the basis

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of the definition of lignans which proposed by McCredie *et al.* [9], they proposed the term of sesquilignan for the first time.

To date, the chemical constituents of only four species ( *Morina longfolia, Morina, M. persica* and *M. kokanica* ) of *Morina* genus plants have been studied,[10-14] sterols, triterpenes, saponins, alkaloids and flavanoids had been found from these plants. As a traditional Chinese medicinal plant, *Morina chinensis* has been used for the treatment of many diseases since ancient times,[15] and has been used as Tibetan medicine too. It is mainly distributed in northwestern of China. In the previous papers,[16-18] we described 16 new phenylpropanol derivatives, morinins A-P, which were isolated from this plant. Now, we wish to report here the isolation and identification of twevel novel neolignan compounds, morinols A-L (**1-12**), along with two known lignans, pinoresinol (**13**) and lariciresinol (**14**) from the roots of this Chinese medicinal herb, as well as the bioactivity results of the isomers, morinols A (**1**) and B (**2**) on cytokine production.

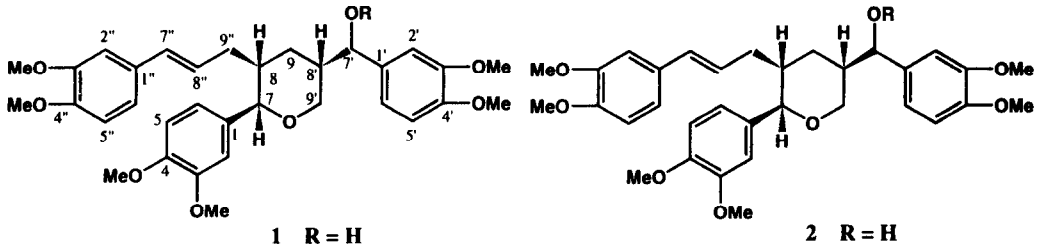
Both of morinols A (**1**) and B (**2**) are containing three $C_6$-$C_3$ units, and they are not linked by a β-β′ bond, so the term of sesquineolignan should be suitable for the type of them. Morinols C-L (**3-12**) should belong to the neolignan compounds. However, all of these new compounds are rare, morinols A (**1**) and B (**2**) bearing a tetrahydropyran ring, with a new carbon skeleton. In morinols C-L (**3-12**), the two $C_6$-$C_3$ units were linked from C-8 (β) to C-9′ (γ′) by a C-C bond directely, this is also the first report of this kind of neolignans. Morinols C-H (**3-8**) were three pairs of *threo* and *erythro* isomers, the chracteristic signals of $^1H$ and $^{13}C$ NMR spectral data were regularly both for *threo* and *erythro* isomers. All of the structures have been identified on the basis of spectral evidences, especially by 2D NMR ($^1H$-$^1H$ COSY, HSQC, HMBC and NOESY) and HRFABMS, as well as chemical transformation. Morinols B (**2**), E (**5**) and G (**7**) were verified should be enantiomeric natural products by means of MTPA and 2NMA.

## RESULTS AND DISCUSSION

Morinol A (**1**), was obtained as a colorless oil. The positive HRFABMS (*m/z* 565.2793, calcd. for $C_{33}H_{41}O_8$, 565.2801 ) showed the molecular formula to be $C_{33}H_{40}O_8$, so its unsaturation value was 14. $^{13}C$ NMR and DEPT spectral data (Table 2) of **1** displayed the presence of three aromatic rings (DEPT indicated nine carbons of aromatic rings were quaternary carbons), a double bond, six methoxyl groups, three methylenes ($\delta_C$ 33.2, C-9; $\delta_C$ 71.0, C-9′; $\delta_C$ 35.8, C-9″) and one of them ($\delta_C$ 71.0, C-9′) should be connected with oxygen atom, four methines ($\delta_C$ 85.5, C-7, 41.9, C-8; $\delta_C$ 77.1, C-7′, 43.5, C-8′) while two of them ($\delta_C$ 85.5, C-7; $\delta_C$ 77.1, C-7′) should be connected with oxygen atoms. It is to say, there were three aromatic rings and other nine carbons except for the six methoxyl groups in compound **1**, just like three $C_6$-$C_3$ units. Furthermore, there must be an another ring except for the three aromatic rings in the structure of **1**, because the unsaturation values of three aromatic rings and the double bond were 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 (**1a**) of compound **1** showed significant down field shift (from $\delta_H$ 4.39 to 5.49) , verified a hydroxyl

group (the existence was further supported by the absorption bands in IR spectrum) must be connected with C-7′. Then, C-7 and C-9′ should be linked by an oxygen atom according to both of the given molecular formula of compound **1** and the chemical shifts of C-7 and C-9′.




**1** R = H
**1a** R = Ac

**2** R = H
**2a** R = Ac

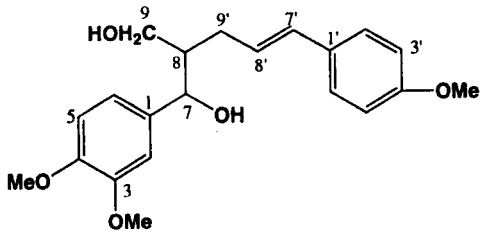
**Fig. 1** The structures of compounds **1** and **2**.

In the HMBC spectrum of **1** (measured in $CD_3OD$ and $CDCl_3$ respectively, because the signal of H-7 was overlapped with the signals of methoxyl groups when $CDCl_3$ was used as solvent), the correlations of H-7 with C-1, C-2, C-6, C-9, C-9″ and C-9′; H-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.

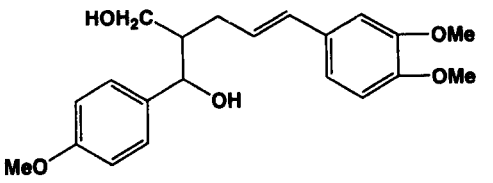
The H-7 and H-8 of **1** was *trans* relationship according to the coupling constant between them ($J_{7,8}$ = 9.6 Hz). The H-8′ should be adopted an *axial* orientation according to both of the spliting pattern and the coupling constants of H-9′α ($\delta_H$ 3.42, 1H, *dd*, *J* = 11.2, 11.2 Hz) and H-9′β ($\delta_H$ 4.38, 1H, *br d*, *J* = 11.2 Hz). 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 of **1**. Hence, the structure of compound **1** has been determined as shown (Figure 1), named as morinol A.

The NMR spectral data of morinol B (**2**) were very similar to those of compound **1**. The chemical shift of H-7′ of the acetate (**2a**) of **2** also showed significant down field shift (from $\delta_H$ 5.07 to 6.10) . The positive HRFABMS (565.2801, calcd. for $C_{33}H_{41}O_8$, 565.2801) of **2** gave a molecular formula of $C_{33}H_{40}O_8$, the same as that of **1**. The evident differences between **1** and **2** were the chemical shifts of H-7′, C-7′, H-9′ and C-9′, especialy the spliting pattern and the coupling constants of H-9 and H-9′.

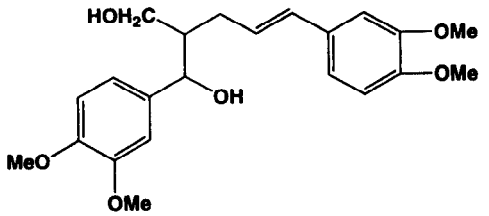
In compound **2**, H-8′ should be adopted a *equatorial* orientation by comparison the spliting pattern and the coupling constants of H-9′α (compound **1**: $\delta_H$ 3.42, 1H, *dd*, *J* = 11.2, 11.2 Hz; compound **2**: $\delta_H$ 3.74, 1H, *dd*, *J* = 11.7, 2.6 Hz) , H-9′β (compound **1**: $\delta_H$ 4.38, 1H, *br d*, *J* = 11.2 Hz; compound **2**: $\delta_H$ 4.05, 1H, *d*, *J* = 11.7 Hz), H-9α (compound **1**: $\delta_H$ 1.13, 1H, *br q*, *J* = 12.0 Hz; compound **2**: $\delta_H$ 1.44, 1H, *ddd*, *J* = 13.0, 13.0, 5.0 Hz) and H-9β (compound **1**: $\delta_H$ 1.70, 1H, *br d*, *J* = 12.0 Hz; compound **2**: $\delta_H$ 1.68, 1H, *br d*, *J* = 13.0 Hz) 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, H-9β and H–8; H-9′α with H-7, H-8′ and H-9α, confirmed the relative configuration furtherly. Thus, compound **2** (Figure 1) was an isomer of **1**, named as morinol B.



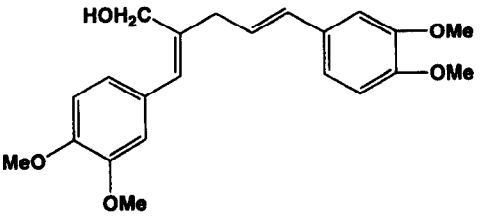
**3** *threo*
**4** *erythro*



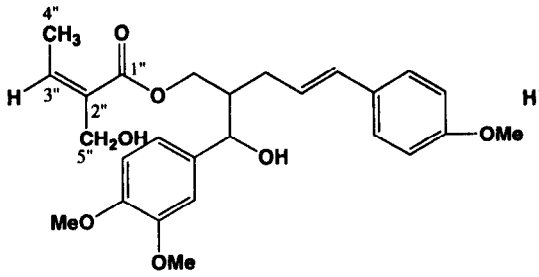
**5** *threo*
**6** *erythro*



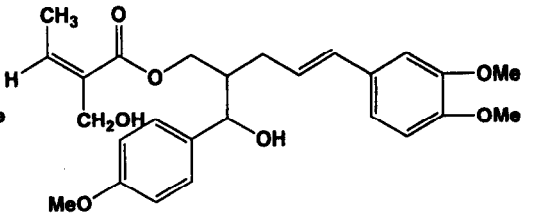
**7** *threo*
**8** *erythro*



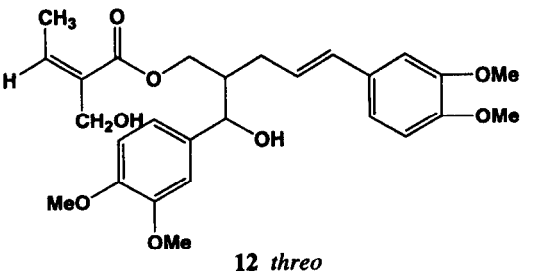
**9**



**10** *threo*



**11** *threo*



**12** *threo*

**Fig. 2** The structures of compounds **3-12.**

**Table 1.** $^1$H NMR spectral data of compounds **1, 2** and **9-12**
(400 MHz, δ, ppm, $CDCl_3$ as solvents)

| H | 1 | 2 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|
| 2 | 6.92, d (1.4) | 6.95, d (1.4) | 7.03, br s | 6.90, d (1.4) | 7.29, d (8.6) | 6.90, br s |
| 3 | | | | | 6.92, d (8.6) | |
| 5 | 6.78, d (8.4) | 6.77, d (8.4) | 6.79, d (8.2) | 6.83, d (8.0) | 6.92, d (8.6) | 6.79, d (8.1) |
| 6 | 6.84, dd (8.4, 1.4) | 6.87, dd (8.4, 1.4) | 6.88, br d (8.2) | 6.88, dd (8.0, 1.4) | 7.29, d (8.6) | 6.83, br d (8.1) |
| 7 | overlapped with OMe | 4.00, d (9.7) | 6.24, s | 4.70, d (6.5) | 4.71, d (6.4) | 4.70, d (6.5) |
| 8 | 1.77, m | 1.98, m | | 2.18, m | 2.18, m | 2.19, m |
| 9 | **1.13, br q (12.0)** | **1.44, ddd (13.0, 13.0, 5.0)** | 4.33, br d (5.6) | 4.30, dd (11.5, 4.2) | 4.30, dd (11.4, 4.2) | 4.29, dd (11.4, 4.2) |
| | **1.70, br d (12.0)** | **1.68, br d (13.0)** | | 4.43, dd (11.5, 3.3) | 4.44, dd (11.4, 3.3) | 4.43, dd (11.4, 3.2) |
| 2′ | 6.89, d (1.4) | 6.72, d (1.3) | 6.71, br s | 7.25, d (9.1) | 6.83, d (1.4) | 6.86, d (1.2) |
| 3′ | | | | 6.82, d (9.1) | | |
| 5′ | 6.73, d (8.5) | 6.75, d (8.5) | 6.88, d (8.2) | 6.82, d (9.1) | 6.79, d (8.1) | 6.79, d (8.1) |
| 6′ | 6.88, dd (8.5, 1.4) | 6.96, dd (8.5, 1.3) | 6.83, br d (8.2) | 7.25, d (9.1) | 6.81, dd (8.1, 1.4) | 6.85, dd (8.1, 1.2) |
| 7′ | 4.39, d (9.1) | 5.07, d (9.0) | 3.55, br d (4.8) | 6.33, d (15.7) | 6.31, d (15.7) | 6.32, d (15.7) |
| 8′ | 2.17, m | 1.92, m | 6.18, dt (16.0, 6.8) | 6.00, dt (15.7, 7.4) | 5.98, dt (15.7, 7.4) | 5.99, dt (15.7, 7.4) |
| 9′ | **4.38, br d (11.2)** | **4.05, d (11.7)** | 6.28, d (16.0) | 2.23, m | 2.22, m | 2.24, m |
| | **3.42, dd (11.2, 11.2)** | **3.74, dd (11.7, 2.6)** | | 2.32, m | 2.31, m | 2.31, m |
| 2″ | 6.91, d (1.3) | 6.95, d (1.4) | | | | |
| 3″ | | | | 6.37, br q (7.2) | 6.38, br q (7.2) | 6.38, br q (7.2) |
| 4″ | | | | 2.12, d (7.2) | 2.12, d (7.2) | 2.12, d (7.2) |
| 5″ | 6.76, d (8.5) | 6.78, d (8.5) | | 4.22, d (12.4) | 4.21, d (12.4) | 4.25, d (12.4) |
| | | | | 4.28, d (12.4) | 4.25, d (12.4) | 4.27, d (12.4) |
| 6″ | 6.87, dd (8.5, 1.3) | 6.89, dd (8.5, 1.4) | | | | |
| 7″ | 6.09, d (15.6) | 6.08, d (15.7) | | | | |
| 8″ | 5.71, dt (15.6, 7.4) | 5.69, dt (15.7, 7.5) | | | | |
| 9″ | 1.80, m; 1.98, m | 1.75, m; 1.97, m | | | | |
| OMe | 3.86 X 3, 3.87, | 3.85, 3.86, 3.87 X 2 | 3.87, 3.88 X 2 | 3.80, 3.88 X 2 | 3.87, 3.88, 3.89 | 3.87, 3.88 X 2 |
| | 3.88 X 2 | 3.88, 3.89 | 3.92 | | | 3.89 |

The data in parentheses are coupling constants in Hz.

The positive HRFABMS of compound **3** gave the quasi-molecular ion peak at *m/z* 359.1826, suggested the molecular formula of $C_{21}H_{26}O_5$. $^1$H NMR spectrum (Table 3) of compound **3** displayed the existence of a *p*-substituted aromatic ring at $\delta_H$ 7.22 (2H, *d*, *J* = 8.7 Hz, H-2′ and 6′) and 6.81 (2H, *d*, *J* = 8.7 Hz, H-3′ and 5′), a 1, 2, 4-trisubstitued aromatic ring at $\delta_H$ 6.92 (1H, *d*, *J* = 1.2 Hz, H-2), 6.83 (1H, *d*, *J* = 8.0 Hz, H-5) and 6.88 (1H, *dd*, *J* = 8.0, 1.2 Hz, H-6), a double bond at $\delta_H$ 6.28 (1H, *d*, *J* = 15.7 Hz, H-7′) and 5.95 (1H, *dt*, *J* = 15.7, 7.4 Hz, H-8′), two methylenes at $\delta_H$ 3.74 (1H, *dd*, *J* = 11.0, 6.4 Hz, H-9), 3.93 (1H, *dd*, *J* = 11.0, 3.6 Hz, H-9), 2.08 (1H, *m*, H-9′) and 2.16 (1H, *m*, H-9′), two methines at $\delta_H$ 4.69 (1H, *d*, *J* = 7.3 Hz, H-7) and 1.99 (1H, *m*, H-8), as well as three methoxy groups at $\delta_H$ 3.79, 3.87 and 3.88. $^{13}$C NMR and DEPT spectral data (Table 4) of compound **3** were further confirmed the above facts.

Both $^1$H and $^{13}$C NMR spectral data of compound **3** showed there were two $C_6$-$C_3$ units except for the methoxyl groups, it seemed to be a lignan compound. In the $^1$H-$^1$H COSY spectrum of **3**, the correlations of H-7

to H-8, H-8 to H-9 and H-9′, H-9′ to H-8′, and H-8′ to H-7′, suggested the given structure. The clear correlations of H-7 to H-2 and H-6, H-7′ to H-2′ and H-6′ in the NOESY spectrum of **3**, verified that the *p*-substituted aromatic ring was connected to the double bond (C-7′), and the other aromatic ring was connected to C-7. These were confirmed by the correlations of HMBC, $\delta_H$ 4.69 (H-7) with $\delta_C$ 109.6 (C-2), 119.0 (C-6), 64.6 (C-9) and 32.2 (C-9′); $\delta_H$ 1.99 (H-8) with $\delta_C$ 136.0 (C-1), 78.5 (C-7) and 125.7 (C-8′); $\delta_H$ 3.74 and 3.93 (H-9) with $\delta_C$ 78.5 (C-7) and 32.2 (C-9′); $\delta_H$ 2.08 and 2.16 (H-9′) with $\delta_C$ 78.5 (C-7), 64.6 (C-9), 131.3 (C-7′) and 125.7 (C-8′); $\delta_H$ 5.95 (H-8′) with $\delta_C$ 130.3 (C-1′) and 47.0 (C-8). The relative configuration of compound **3** should be *threo* according to the coupling constant of H-7 ($J_{7,8}$ = 7.3 Hz)[19,20] and the chemical shift of C-7 ($\delta_C$ 78.5). Thus, the structure of morinol C has been determined as shown (Figure 2).

**Table 2.** $^{13}C$ NMR and DEPT spectral data of compounds **1, 2** and **9-12.**
(100 MHz, δ, ppm, $CDCl_3$ as solvents)

| C | 1 | 2 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|
| 1 | 133.6 s | 133.6 s | 130.7 s | 135.3 s | 134.8 s | 135.3 s |
| 2 | 109.3 d | 109.0 d | 109.2 d | 109.4 d | 127.7 d | 109.5 d |
| 3 | [a]149.1 s | [a]148.9 s | [a]149.0 s | [a]148.7 s | 114.1 d | [a]148.7 s |
| 4 | [a]149.2 s | [a]149.0 s | [a]149.2 s | [a]149.3 s | 159.4 s | [a]148.8 s |
| 5 | [b]111.1 d | [b]111.1 d | 111.3 d | 111.2 d | 114.1 d | [b]111.1 d |
| 6 | 118.8 d | 118.9 d | 119.2 d | 118.8 d | 127.7 d | 118.8 d |
| 7 | 85.5 d | 85.9 d | 130.6 d | 75.3 d | 75.2 d | 75.3 d |
| 8 | 41.9 d | 38.4 d | 130.3 s | 45.4 d | 45.4 d | 45.4 d |
| 9 | 32.2 t | 31.9 t | 64.2 t | 63.7 t | 63.7 t | 63.7 t |
| 1′ | 135.5 s | 136.4 s | 128.1 s | 130.2 s | 130.6 s | 130.5 s |
| 2′ | 110.3 d | [b]110.7 d | 113.1 d | 127.2 d | 108.8 d | 108.8 s |
| 3′ | [a]148.8 s | [a]149.1 s | 147.8 s | 114.1 d | [a]148.7 s | [a]149.1 s |
| 4′ | [a]149.0 s | [a]149.3 s | 148.6 s | 159.0 s | [a]149.1 s | [a]149.3 s |
| 5′ | [b]110.9 d | [b]111.2 d | 109.2 d | 114.1 d | 111.3 d | [b]111.3 d |
| 6′ | 120.3 d | 120.0 d | 128.9 d | 127.2 d | 119.1 d | 119.1 d |
| 7′ | 77.1 d | 74.0 d | 36.2 t | 131.9 d | 132.1 d | 132.1 d |
| 8′ | 43.5 d | 41.7 d | 128.5 d | 125.1 d | 125.5 d | 125.4 d |
| 9′ | 71.0 t | 68.7 t | 127.2 d | 32.3 t | 32.3 t | 32.3 t |
| 1″ | 130.7 s | 130.7 s | | 166.8 s | 166.8 s | 166.8 s |
| 2″ | 108.5 d | 108.6 d | | 131.9 s | 132.0 s | 131.9 s |
| 3″ | [a]148.4 s | [a]148.4 s | | 142.2 d | 142.1 d | 142.2 d |
| 4″ | [a]148.7 s | [a]148.6 s | | 15.8 q | 15.8 q | 15.8 q |
| 5″ | [b]110.9 d | [b]110.7 d | | 65.5 t | 65.6 t | 65.5 t |
| 6″ | 118.8 d | 118.1 d | | | | |
| 7″ | 131.2 d | 131.2 d | | | | |
| 8″ | 125.7 d | 125.5 d | | | | |
| 9″ | 35.8 t | 35.7 t | | | | |
| OMe | 55.8, 55.9 X 2 | 55.8 X 2, 55.9 X 2 | 55.3, 55.9, 56.0 | 55.4, 56.0 X 2 | 55.4, 55.9, 56.0 | 55.9, 56.0 X 3 |
| | 56.0 X 3 | 56.0, 56.1 | | | | |

[a, b]The assignments maybe be interchangeble in the same column.

The $^1H$ (Table 3) and $^{13}C$ NMR (Table 4) spectral data of compound **4** were nearly identical with those of **3**, its positive HRFABMS gave the molecular ion peak at *m/z* 359.1859, consistant with the same molecular formula of $C_{21}H_{26}O_5$ as that of **3**. The evident differences between compounds **3** and **4** were that the coupling constants of H-7 (Compound **3**: $J_{7,8}$ = 7.3 Hz; Compound **4**: $J_{7,8}$ = 4.5 Hz)[19, 20] and the chemical shifts of C-7 (Compound **3**: $\delta_C$ 78.5; Compound **4**: $\delta_C$ 76.4). These verified compound **4** was the *erythro* isomer of compound **3**, named as morinol D.

The positive HRFABMS of compound **5** gave the molecular ion peak at *m/z* 359.1811, suggested the same molecular formula of $C_{21}H_{26}O_5$ as those of **3** and **4**. The $^1H$ (Table 3) and $^{13}C$ NMR (Table 4) spectral data of **5** were very similar to those of compound **3**. However, in the NOESY spectrum of compond **5**, the clear correlations of H-7 to H-2 and H-6, H-7′ to H-2′ and H-6′ , verified that the *p*-substituted aromatic ring was connected to C-7, and the other aromatic ring was connected to the double bond (C-7′). These linkages were confirmed by the correlations of HMBC, $\delta_H$ 4.68 (H-7) with $\delta_C$ 127.8 (C-2 and C-6), 64.6 (C-9) and 32.2 (C-9′); $\delta_H$ 1.98 (H-8) with $\delta_C$ 135.5 (C-1), 78.3 (C-7) and 126.0 (C-8′); $\delta_H$ 5.92 (H-8′) with $\delta_C$ 130.7 (C-1′) and 47.0 (C-8). The relative configuration of compound **5** was also should be *threo* according to the coupling constant of H-7 ($J_{7,8}$ = 7.4 Hz)[19, 20] and the chemical shift of C-7 ($\delta_C$ 78.3). Thus, the structure of morinol E has been determined as shown.

The $^1H$ (Table 3) and $^{13}C$ NMR (Table 4) spectral data of **6** were nearly identical with those of **5**, its positive HRFABMS gave the molecular ion peak at *m/z* 359.1857, suggested the same molecular formula of $C_{21}H_{26}O_5$ as that of **5**. Similar to the differences between compounds **4** and **3**, the evident differences between compounds **6** and **5** were also that the coupling constants of H-7 (Compound **5**: $J_{7,8}$ = 7.4 Hz; Compound **6**: $J_{7,8}$ = 4.4 Hz) and the chemical shifts of C-7 (Compound **5**: $\delta_C$ 78.3; Compound **6**: $\delta_C$ 76.4). Hence, morinol F was the *erythro* isomer of compound **5**.

The NMR spectral data of compounds **7** and **8** showed both aromatic rings of them were 1, 2, 4 -trisubstituted, and four methoxyl groups were displayed while there were only three for **3-6**. The positive HRFABMS of compounds **7** (*m/z* 389.1963) and **8** (*m/z* 389.1954) showed they had the same molecular formula of $C_{22}H_{28}O_6$. The NMR spectral data of compounds **7** and **8** not only very similar, but also showed they were another pair of isomers (Compound **7**, *threo*: $J_{7,8}$ = 7.3 Hz, $\delta_{C\text{-}7}$ 78.1; compound **8**, *erythro* : $J_{7,8}$ = 4.4 Hz, $\delta_{C\text{-}7}$ 76.4). We named compounds **7** and **8** as morinols G and H, respectively.

Both $^1H$ (Table 1) and $^{13}C$ NMR (Table 2) spectral data showed compound **9** bearing two pairs of double bonds (C-7, C-8; C-8′, C-9′) and two methylenes (C-7′, C-9) while a hydroxyl group should be connected with C-9 ($\delta_C$ 64.2). Its FABMS gave the quasi-molecular ion peak at *m/z* 393 $[M+Na]^+$, which, together with its NMR spectral data, suggested the molecular formula was $C_{22}H_{26}O_5$. In the HMBC spectrum of **9**, the correlations of $\delta_H$ 6.24 (H-7) with $\delta_C$ 130.7 (C-1), 109.2 (C-2), 119.2 (C-6), 130.3 (C-8) and 64.2 (C-9); $\delta_H$ 3.55 (H-7′) with

$\delta_C$ 128.1 (C-1′), 113.1 (C-2′), 128.5 (C-8′) and 127.2 (C-9′), verified the structure as shown. In the NOESY spectrum, the correlations of $\delta_H$ 3.55 (H-7′) with $\delta_H$ 6.71 (H-2′), 6.83 (H-6′), 6.18 (H-8′) and 6.28 (H-9′); $\delta_H$ 6.24 (H-7) with $\delta_H$ 7.03 (H-2), 6.86 (H-6) and 6.28 (H-9′), confirmed not only the determined linkages but also the shown relative configurations of the two pairs of double bonds. Named compound **9** as morinol I.

**Table 3.** $^1$H NMR spectral data of compounds **3-8**.
(400 MHz, δ, ppm, $CDCl_3$ as solvents)

| H | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|
| 2 | 6.92, d (1.2) | 6.95, d (1.4) | 7.29, d (8.6) | 7.32, d (8.6) | 6.86, d (1.1) | 6.96, d (1.3) |
| 3 | | | 6.89, d (8.6) | 6.92, d (8.6) | | |
| 5 | 6.83, d (8.0) | 6.87, d (8.2) | 6.89, d (8.6) | 6.92, d (8.6) | 6.73, d (8.2) | 6.81, d (8.1) |
| 6 | 6.88, dd (8.0, 1.2) | 6.94, dd (8.2, 1.4) | 7.29, d (8.6) | 7.32, d (8.6) | 6.80, dd (8.2, 1.0) | 6.92, dd (8.1, 1.3) |
| 7 | **4.69, d (7.3)** | **4.98, d (4.5)** | **4.68, d (7.4)** | **5.00, d (4.4)** | **4.59, d (7.3)** | **5.00, d (4.4)** |
| 8 | 1.99, m | 2.08, m | 1.98, m | 2.08, m | 1.90, m | 2.07, m |
| 9 | 3.74, dd (11.0, 6.4) | 3.74, dd (11.0, 6.4) | 3.72, dd (11.0, 6.4) | 3.74, dd (11.0, 6.4) | 3.65, dd (10.9, 6.4) | 3.77, m |
| | 3.93, dd (11.0, 3.6) | | 3.89, dd 11.0, 3.0) | | 3.81 (Overlapped) | |
| 2′ | 7.22, d (8.7) | 7.24, d (8.4) | 6.83, d (1.5) | 6.86, d (1.2) | 6.79, d (1.2) | 6.87, d (1.2) |
| 3′ | 6.81, d (8.7) | 6.83, d (8.4) | | | | |
| 5′ | 6.81, d (8.7) | 6.83, d (8.4) | 6.78, d (8.1) | 6.79, d (8.1) | 6.72, d (8.2) | 6.82, d (8.1) |
| 6′ | 7.22, d (8.7) | 7.24, d (8.4) | 6.81, dd (8.1, 1.5) | 6.82, dd (8.1, 1.2) | 6.75, dd (8.2, 1.2) | 6.86, dd (8.1, 1.2) |
| 7′ | 6.28, d (15.7) | 6.36, d (15.8) | 6.25, d (15.7) | 6.33, d (15.8) | 6.20, d (15.7) | 6.35, d (15.7) |
| 8′ | 5.95, dt (15.7, 7.4) | 6.03, dt (15.8, 7.4) | 5.92, dt (15.7, 7.4) | 6.01, dt (15.8, 7.4) | 5.88, dt (15.7, 7.4) | 6.02, dt (15.7, 7.4) |
| 9′ | **2.08, m** | **2.29, m** | **2.09, m** | **2.27, m** | **2.01, m** | **2.30, m** |
| | **2.16, m** | | **2.13, m** | | **2.09, m** | |
| OMe | 3.79, 3.87, 3.88 | 3.80, 3.85, 3.87 | 3.80, 3.89, 3.90 | 3.82, 3.87, 3.89 | 3.77, 3.78, 3.80X2 | 3.87, 3.88, 3.89, 3.90 |

The data in parentheses are coupling constants in Hz.

The NMR spectral data of compound **10** were very similar to those of compound **3**. However, both $^1$H and $^{13}$C NMR spectral data of compound **10** exibited that it born an oxygenated angeloyl group. Comparison the $^1$H NMR spectral data of **3** and **10**, the evident difference was the the chemical shift of H-9 of **10** showed significant downfield shifted than that of **3**. In the HMBC spectrum of compound **10**, the evident correlation of $\delta_H$ 4.30 and 4.43 (H-9) with $\delta_C$ 166.8 (carbonyl carbon of angeloyl group) further confirmed the angeloyl group was connected with C-9. The positive HRFABMS of compound **10** (*m/z* 457.2221) gave the corresponding molecular formula of $C_{26}H_{32}O_7$. The coupling constant of H-7 ($J_{7,8}$ = 6.5 Hz) also showed the relative stereochmistry configuration was *threo*. Named this compound as morinol J.

The NMR spectral data of compounds **11** and **12** showed they were aslo the same kind of neolignan copmounds as morinol J (**10**). The differences between them were the subsituted situations of aromatic rings, compounds **11** and **12** were as same as those of compounds **5** and **7**, respectively, while compound **10** was as

same as that of compound **3**. Both compound **11** and **12** were the *threo* relative stereochmistry configurations according to their coupling constants of H-7, and their structures were confirmed by HRFABMS and 2D NMR. We named compounds **11** and **12** as morinols K and L, respectively.

The known compounds pinoresinol (**13**)[21,22] and lariciresinol (**14**)[21,23] were identified by comparison of their $^1H$ and $^{13}C$ NMR spectral data with those reported in the literatures, and confirmed by 2D NMR ($^1H$-$^1H$ COSY, NOESY, HSQC and HMBC) furtherly.

**Table 4.** $^{13}C$ NMR and DEPT spectral data of compounds **3-8**.
(100 MHz, δ, ppm, $CDCl_3$ as solvents)

| C | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|
| 1 | 136.0 s | 135.2 s | 135.5 s | 134.6 s | 135.9 s | 135.2 s |
| 2 | 109.6 d | 109.6 d | 127.8 d | 127.5 d | 109.5 d | 109.5 d |
| 3 | 148.7 s | 148.5 s | 113.9 d | 113.9 d | [b]148.2 s | [a]148.6 s |
| 4 | 149.2 s | 149.1 s | 159.3 s | 159.1 s | [b]148.8 s | [a]149.2 s |
| 5 | 111.0 d | 111.1 d | 113.9 d | 113.9 d | 111.1 d | [b]111.3 d |
| 6 | 119.0 d | 118.5 d | 127.8 d | 127.5 d | [a]118.8 d | 119.0 d |
| 7 | **78.5 d** | **76.4 d** | **78.3 d** | **76.4 d** | **78.1 d** | **76.4 d** |
| 8 | 47.0 d | 47.2 d | 47.0 d | 47.1 d | 46.6 d | 47.2 d |
| 9 | 64.6 t | 64.0 t | 64.6 t | 64.0 t | 64.3 t | 64.1 t |
| 1′ | 130.3 s | 130.4 s | 130.7 s | 130.8 s | 130.4 s | 130.7 s |
| 2′ | 127.1 d | 127.2 d | 108.7 d | 108.7 d | 108.5 d | 108.7 d |
| 3′ | 114.0 d | 114.1 d | 148.5 s | 148.5 s | [b]148.3 s | [a]148.5 s |
| 4′ | 158.9 s | 159.0 s | 149.1 s | 149.1 s | [b]148.8 s | [a]149.1 s |
| 5′ | 114.0 d | 114.1 d | 111.3 d | 111.3 d | 110.8 d | [b]111.1 d |
| 6′ | 127.1 d | 127.2 d | 119.0 d | 119.0 d | [a]118.7 d | 118.5 d |
| 7′ | 131.3 d | 131.2 d | 131.5 d | 131.5 d | 131.2 d | 131.5 d |
| 8′ | 125.7 d | 126.5 d | 126.0 d | 126.8 d | 125.9 d | 126.8 d |
| 9′ | **32.2 t** | **29.5 t** | **32.2 t** | **29.4 t** | **31.9 t** | **29.4 t** |
| OMe | 55.3, 56.0 X 2 | 55.4, 56.0 X 2 | 55.3, 55.9, 56.0 | 55.4, 55.9, 56.0 | 55.6, 55.7 X 3 | 55.9, 56.0 X 3 |

[a, b]The assignments maybe be interchangeble in the same column.

The (R)- and (S)-MTPA esters of of compound **2** were prepared using modified Mosher's method. However, the $^1H$ NMR spectra of both (R)- and (S)-MTPA esters displayed separated pairs of signals, and the signals of H-7′ [In **2**: $\delta_H$ 5.07; in (R)-MTPA ester: $\delta_H$ 6.40 and 6.27; in (S)-MTPA ester: $\delta_H$ 6.40 and 6.27] were the most evident. This result indicated compound **2** should be a racemic natural product, and the ratio of two enantiomer isomers is about 1:1 according to the integrals of the separated proton signals. Due to both compound **5** and **7** bear two free hydroxyl groups, we first locked their 9-hydroxyl groups by acetylation using acetic anhydride

and pyridine in ice-bath for 15 minutes, and their 9-monoacetates were obtained. After that, the 9-monoacetates of **5** and **7** were treated with another new chiral anisotropic reagent, 2NMA,[24,25] gave the (R)- and (S)-2NMA esters of each 9-monoacetate. However, just like the $^1$H NMR spectra of (R)- and (S)-MTPA esters of **2**, all of the $^1$H NMR spectra of (R)- and (S)-2NMA esters of 9-monoacetate of **5** and **7** showed they also should be racemic mixtures, and the ratios of two enantiomer isomers for **5** an **7** are still about 1:1. The structure of compound **1** is very similar to that of **2**, while **3, 4, 6, 8, 10-12** are very similar to those of **5** and **7**. Furthermore, the optical rotation values of all these compounds are near zero, so the others maybe also racemic mixtures.

The induction of cytokines in human peripheral blood mononuclear cells by various species of mycoplasmas[26] and the interleukin-1α (IL-1α) and 1β (IL-1β) production in peripheral whole blood from patients with urological cancer[27] have been reported. We examined the abilities to reduce cytokine production of the isomers, morinols A (**1**) and B (**2**), the results indicated that morinol B (**2**) has more strong activity than its isomer, morinol A (**1**). The percentage inhibition of compounds **1** and **2** on cytokines gave in Table 5.

**Table 5.** Percentage Inhibition of Compounds **1** and **2** on cytokines

| Compounds | Concentration | TNF-α | IL-8 | IL-1β | IL-4 | IL-2 | IFN-γ |
|---|---|---|---|---|---|---|---|
| **1** | 10 μg/ml | -48.9 | 46.1 | 13.4 | 13.9 | **62.0** | 24.8 |
| **2** | 10 μg/ml | **70.5** | -24.9 | 32.5 | **96.9** | **91.0** | **97.9** |
| | 3 μg/ml | 46.1 | 13.6 | 19.6 | **61.7** | **67.4** | **61.3** |
| | 1 μg/ml | 18.2 | 16.5 | 4.4 | 25.3 | 32.0 | 30.3 |
| Predonisolon | 0.3 μg/ml | 60.0 | 39.1 | 67.9 | 98.0 | 94.9 | 96.4 |

## EXPERIMENTAL SECTION

**General Experimental Procedures.**

NMR (400 MHz for $^1$H NMR, 100 MHz for $^{13}$C NMR, both use TMS as int. stand.) were measured on a Bruker AM 400 spectrometer and MS spectra on a JEOL JMSD-300 instrument; CC: silica gel 60 (Merck); HPLC: GPC (shodex H-2001, 2002, $CHCl_3$), Silica gel (Si 60, Hibar RT 250-25). IR spectra were recorded on a 1720 Infrared Fourier Transform spectrometer (PERKIN-ELMER), UV spectra on a UV2100 UV-Vis recording spectrometer (shimadzu). Optical rotation were measured with a JASCO DIP-370 digital polarimeter.

**Plant Material.**

The whole plants (including 1.8 kg roots and 3.0 kg stems and leaves) of *Morina chinensis* was collected in the south of Qinghai province, China, in August 1998. It was identified by Dr. Wang Hengshan, Department of Biology, Lanzhou University, China. The voucher specimen has been preserved at the Herbarium of the Faculty of Pharmaceutical Sciences, University of Tokushima, Japan.

**Extraction and Isolation of Compounds.**

The powders of air dried roots of *Morina chinensis* were extracted with MeOH (15 L each time) at the temprature about 60 $^0$C for three times, 6 hours for each time. After concentration of the combined extracts under reduced pressure, the residue (200 g) was diluted with water, and then extracted with $CHCl_3$ and *n*-butanol, respectively.

The $CHCl_3$ extract (120 g) was chromatographed over a silica gel column (11 x 100 cm, Merck silica gel 60, 1.6 kg) and eluted with *n*-hexane-acetone (15:1 to 1:1, then use pure acetone and MeOH eluted, respectively). Thirteen fractions were obtained.

Fraction 12 (6.32 g) was chromatographed over a mid-pressure silica gel column (3.5 x 45 cm) and eluted with $CHCl_3$-MeOH (from 50:1 to 4:1), to give 10 fractions (Fr12.1-Fr12.10). The mixture (570 mg) of Fr12.1 and Fr12.2 was chromatographed over a silica gel column (3.5 x 60 cm), and eluted with *n*-hexane-EtOAc (3:1), to give 2 fractions (Fr12.1.1-Fr12.1.2). Fr12.1.2 (370 mg) was chromatographed over a silica gel column (3.5 x 60 cm), and eluted with *n*-hexane-acetone (from 4:1 to 1:1), obtained 7 fractions (Fr12.1.2.1-Fr12.1.2.7) furtherly. Then, Fr12.1.2.6 (140 mg) was isolated by HPLC (silica, *n*-hexane-EtOAc, 2:5), obtained compounds **1** (61 mg) and **2** (37 mg). Fr12.1.2.3 was further chromatographed over a silica gel column (3.3 x 60 cm), and eluted with *n*-hexane-EtOAc (4:1 to 1:2), to give 4 fractions (Fr12.1.2.3.1-Fr12.1.2.3.4). Compounds **13** (17 mg) and **9** (5 mg) were obtaine after the purification of Fr12.1.2.3.1 by using GPC ($CHCl_3$).The mixture (1.02 g) of Fr12.3-Fr12.6 was chromatographed over a silica gel column (3.5 x 65 cm) and eluted with $CHCl_3$-MeOH (20:1), to give 3 fractions (Fr12.3.1-Fr12.3.3). Fr 12.3.2 (450 mg) was isolated by HPLC (silica, *n*-hexane-EtOAc, 1:3), to gave pure compound **7** (38 mg) and other 25 fractions (Fr12.3.2.1-Fr12.3.2.25). Compounds **6** (6 mg) and **11** (8 mg) were obtained after the purification of Fr12.3.2.17 by using GPC ($CHCl_3$). Compound **4** (2.5 mg) was obtained from Fr12.3.2.18, compound **10** (2.5 mg) was obtained from Fr12.3.2.19, compound **5** (15 mg) was obtained from Fr12.3.2.20, compound **3** (12 mg) was obtained from Fr12.3.2.22, compounds **8** (6 mg) and **12** (11 mg) were obtained from Fr12.3.2.25 after the purifications by using GPC ($CHCl_3$). Fr 12.3.3 (410 mg) was isolated by HPLC (silica, *n*-hexane-EtOAc, 1:5), to gave 14 fractions (Fr12.3.3.1-Fr12.3.3.14), compound **14** (15 mg) was obtained after the purification of Fr12.3.3.8 by using GPC ($CHCl_3$).

**Morinol A (1)** Obtained as a colorless oil. $[\alpha]_D^{25}$ +0.98$^0$ ( *c* 1.016; $CHCl_3$ ); IR (KBr) $\nu_{max}$ cm$^{-1}$: 3856, 3478, 3435, 2362, 2343, 1656, 1639, 1511, 1265, 1140, 1028, 670; UV $\lambda_{max}^{CHCl3}$ nm (log$\varepsilon$): 272.5 (3.94), 240.2 (3.93). $^1$H NMR spectral data of **1** (400 MHz, $\delta$, ppm, $CD_3OD$): 6.03 (1H, *d*, *J* = 15.6 Hz, H-7″), 5.67 (1H, *dt*, *J* = 15.6,

7.2 Hz, H-8″), 4.28 (1H, *d*, J = 8.2 Hz, H-7′), 4.34 (1H, *br d*, J = 10.2 Hz, H-9′β), 3.89 (1H, *d*, J = 9.6 Hz, H-7), 3.40 (1H, *t*, *J* = 11.0 Hz, H-9′α), 2.07 (1H, *m*, H-8′), 1.90 (1H, *m*, H-9″β), 1.75 (1H, *m*, H-9″α), 1.74 (1H, *m*, H-8), 1.58 (1H, *br d*, *J* = 12.6 Hz, H-9β), 1.07 (1H, *br q*, *J* = 12.0 Hz, H-9″α), 3.76, 3.77, 3.78, 3.79, 3.80 (OMe), 6.66-6.96 (9H, Ar-H). $^{13}$C NMR spectral data of **1** (100 MHz, δ, ppm, $CD_3OD$):150.4×2, 150.3×2, 149.8, 149.7 (s, C-3, C-4, C-3′, C-4′, C-3″, C-4″), 137.5 (s, C-1′), 135.0 (s, C-1), 132.4 (s, C-1″), 132.2 (d, C-7″), 126.9 (d, C-8″), 121.8 (d, C-6′), 120.3, 120.2 (d, C-6, C-6″), 112.7, 112.5, 112.4, 112.3 (d, C-2′, C-5, C-5′, C-5″), 111.4 (d, C-2″), 109.9 (d, C-2), 87.0 (d, C-7), 77.5 (d, C-7′), 72.4 (t, C-9′), 56.3, 56.4 (OMe), 45.0 (d, C-8′), 43.2 (d, C-8), 37.0 (t, C-9″), 34.6 (C-9); The $^1$H and $^{13}$C NMR data of **1** measured in $CDCl_3$ see Table 1 and Table 2, respectively; The positive HRFABMS: *m/z* 565.2793 (calcd. for $C_{33}H_{41}O_8$, 565.2801). FABMS (*m/z*): 565, 564, 547, 485, 460, 399, 359, 307, 289, 273, 177, 154 (base peak), 137, 136, 107, 77, 39.

**Acetate of morinol A (1a)** Morinol A (5 mg) was acetylated with acetic anhydride (0.5 ml) and pyridine (0.5 ml) at room temprature overnight. The products was purified by using PTLC (Merck, 20 X 20 cm) and eluted with hexane-EtOAc (1:2), obtained the pure acetate of morinol A (**1a**). $^1$H NMR spectral data of **1a** (400 MHz, δ, ppm, $CDCl_3$): 6.08 (1H, *d*, *J* = 15.6 Hz, H-7″), 5.71 (1H, *dt*, *J* = 15.6, 7.2 Hz, H-8″), 5.49 (1H, *d*, *J* = 8.6 Hz, H-7′), 4.22 (1H, *dd*, *J* = 11.0, 0.9 Hz, H-9′β), 3.37 (1H, *t*, *J* = 11.0 Hz, H-9′α), 2.35 (1H, *m*, H-8′), 2.07 (3H, *s*, $OCCH_3$), 1.97 (1H, *m*, H-9″β), 1.77 (1H, *m*, H-9″α), 1.79 (1H, *m*, H-8), 1.71 (1H, *br d*, *J* = 13.2 Hz, H-9β), 1.10 (1H, *br q*, *J* = 12.2 Hz, H-9″α), 3.85, 3.86, 3.88 (OMe), 6.06-6.88 (9H, Ar-H).

**Morinol B (2)** Obtained as a colorless oil. $[\alpha]_D^{25}$ -3.92° ( *c* 0.510; $CHCl_3$ ); IR (KBr) $\nu_{max}$ cm$^{-1}$: 3856, 3652, 3632, 3478, 3436, 2364, 2346, 1655, 1639, 1510, 1460, 1264, 1140, 1028, 570; UV $\lambda_{max}^{CHCl_3}$ nm (logε): 272.5 (3.95), 241.4 (3.89); The positive HRFABMS: *m/z* 565.2801 (calcd. for $C_{33}H_{41}O_8$, 565.2801); FABMS (*m/z*): 565, 564, 547, 499, 453, 399, 358, 307, 289, 287, 273, 177 (base peak), 151, 136, 107, 91, 77, 39; $^1$H and $^{13}$C NMR data see Table 1 and Table 2, respectively.

**Acetate of morinol B (2a)** Morinol B (5 mg) was acetylated by using the same method as that of acetalation of morinol A, obtained the pure acetate of morinol B (**2a**). $^1$H NMR spectral data of **2a** (400 MHz, δ, ppm, $CDCl_3$): 6.10 (1H, *d*, *J* = 10.6 Hz, H-7′), 6.07 (1H, *d*, *J* = 15.6 Hz, H-7″), 5.67 (1H, *dt*, *J* = 15.6, 7.1 Hz, H-8″), 4.26 (1H, *br d*, *J* = 11.7 Hz, H-9′β), 4.00 (1H, *d*, *J* = 9.4 Hz, H-7), 3.73 (1H, *dd*, *J* = 11.7, 1.9 Hz, H-9′α), 2.13 (1H, *m*, H-8′), 2.06 (3H, *s*, $OCCH_3$), 1.96-2.01 (2H, *m*, H-8 and H-9″β), 1.74 (1H, *m*, H-9″α), 1.61 (1H, *br d*, *J* = 13.3 Hz, H-9β), 1.43 (1H, *ddd*, *J* = 13.3, 12.1, 4.6 Hz, H-9″α), 3.78, 3.82, 3.85, 3.86, 3.89, 3.95 (OMe), 6.68-6.98 (9H, Ar-H).

**(R)- and (S)-MTPA esters of morinol B (2)** Morinol B (1.0 mg) was treated with (R)-MTPA (3.5 mg) and 2, 4, 6-trinitrochlorobenzene (4.5 mg) in dried pyridine (0.2 ml) at room temperature. After the mixture was stirred for 20 h, added 3 ml 5% aqueous sodium hydrogen carbonate and 5 ml ether in the mixture. The organic layer was successively washed with $H_2O$, 5% aqueous $NaHCO_3$, 5% aqueous $CuSO_4$, and brine. After removed

the solvent, the residue was purified by PTLC, (R)-MTPA ester of morinol B was obtained. By the same way, another portion (1.0 mg) of morinol B was treated with (S)-MTPA, gave (S)-MTPA ester. $^1$H NMR data of (R)-MTPA ester (400 MHz, δ, ppm, $CDCl_3$): 6.62-7.01 (18H, Ar-H), 6.40 (1H, *d*, *J* = 10.0 Hz, H-7′), 6.27 (1H, *d*, *J* = 10.0 Hz, H-7′), 6.08 (1H, *d*, *J* = 15.9 Hz, H-7″), 6.07 (1H, *d*, *J* = 15.9 Hz, H-7″), 5.65 (2H, m, H-8″), 4.28 (2H, *br d*, *J* = 11.8 Hz, H-9′a), 4.03 (2H, *br d*, *J* = 9.7 Hz, H-7), 3.98, 3.96, 3.94, 3.92, 3.91, 3.90, 3.89, 3.86, 3.85, 3.81, 3.80, 3.79 (each 3H, *s*, OMe), 3.73 (2H, *m*, H-9′b), 2.18 (2H, *m*, H-8′), 1.98-2.05 (4H, *m*, H-8 and H-9″b), 1.72 (2H, *m*, H-9″a), 1.60 (1H, *d*, *J* = 13.2 Hz, H-9a), 1.59 (1H, *d*, *J* = 13.2 Hz, H-9a), 1.45 (2H, *m*, H-9b). The $^1$H NMR data of (S)-MTPA ester are the same as those of (R)-MTPA ester.

**Morinol C (3)** Obtained as a colorless oil. $[\alpha]_D^{24}$ -1.7° ( *c* 1.05; $CHCl_3$ ); IR (KBr) $\nu_{max}$ cm$^{-1}$: 3401, 2363, 1562, 1544, 1511, 1267, 827; UV $\lambda_{max}^{CHCl_3}$ nm (log$\varepsilon$): 240.1 (sh, 3.83), 271.6 (br, 3.92); The positive HRFABMS: *m/z* 359.1826 (calcd. for $C_{21}H_{27}O_5$, 359.1858 ); FABMS (*m/z*): 359, 358, 340, 309, 237, 210, 165, 147 (base peak), 121, 91, 77, 55, 41; $^1$H NMR data see Table 3; $^{13}$C NMR and DEPT data see Table 4.

**Morinol D (4)** Obtained as a colorless oil. $[\alpha]_D^{24}$ +0.8° ( *c* 0.25; $CHCl_3$ ); IR (KBr) $\nu_{max}$ cm$^{-1}$: 3413, 1516, 1467, 1267, 1178, 1157, 1140, 1023, 827, 795; UV $\lambda_{max}^{CHCl_3}$ nm (log$\varepsilon$): 240.4 (sh, 3.79), 271.5 (br, 3.87); The positive HRFABMS: *m/z* 359.1859 (calcd. for $C_{21}H_{27}O_5$, 359.1858); FABMS (*m/z*): 359, 358, 341, 309, 233, 210, 192, 165, 147 (base peak), 121, 91, 77, 55, 41; $^1$H NMR data see Table 3; $^{13}$C NMR and DEPT data see Table 4.

**Morinol E (5)** Obtained as a colorless oil. $[\alpha]_D^{24}$ -0.4° ( *c* 0.95; $CHCl_3$ ); IR (KBr) $\nu_{max}$ cm$^{-1}$: 3953, 3737, 3621, 1516, 1468, 1267, 1140, 1023, 795; UV $\lambda_{max}^{CHCl_3}$ nm (log$\varepsilon$): 240.6 (sh, 3.82), 271.6 (br, 3.91); The positive HRFABMS: *m/z* 359.1811 (calcd. for $C_{21}H_{27}O_5$, 359.1858); FABMS (*m/z*): 359, 358, 341, 309, 257, 233, 205, 177 (base peak), 151, 135, 121, 91, 69, 55, 41; $^1$H NMR data see Table 3; $^{13}$C NMR and DEPT data see Table 4.

**Acetylation of morinol E (5)** 5.8 mg Morinol E was acetylated use an excess of acetic anhydride (0.1 ml) in pyridine (0.1 ml) at 0 °C for 15 min, then added 1 ml MeOH to the mixture. The residue was purified by PTLC after removed the solvents, and gave diacetate of morinol E (1.8 mg), 9-monoacetate of morinol E (2.2 mg) and the remaining morinol E (1.5 mg). $^1$H NMR spectral data of diacetate of morinol E (400 MHz, δ, ppm, $CDCl_3$): 7.28 (2H, *d*, *J* = 8.6 Hz, H-2 and H-6), 6.90 (2H, *d*, *J* = 8.6 Hz, H-3 and H-5), 6.80-6.84 (3H, *m*, H-2′, H-5′ and H-6′), 6.23 (1H, *d*, *J* = 15.8 Hz, H-7′), 5.90 (1H, *dt*, *J* = 15.8, 7.4 Hz, H-8′), 5.77 (1H, *d*, *J* = 7.5 Hz, H-7), 4.31 (1H, *dd*, *J* = 11.2, 5.2 Hz, H-9a), 4.11 (1H, *dd*, *J* = 11.2, 4.4 Hz, H-9b), 3.89, 3.87, 3.80 (each 3H, *s*, OMe), 2.35 (1H, *m*, H-8), 2.09-2.18 (2H, *m*, H-9′), 2.05, 2.06 (each 3H, $COCH_3$); $^1$H NMR spectral data of 9-monoacetate of morinol E (400 MHz, δ, ppm, $CDCl_3$): 7.28 (2H, *d*, *J* = 8.6 Hz, H-2 and H-6), 6.90 (2H, *d*, *J* = 8.6 Hz, H-3 and H-5), 6.80-6.84 (3H, *m*, H-2′, H-5′ and H-6′), 6.24 (1H, *d*, *J* = 15.8 Hz, H-7′), 5.93 (1H, *dt*, *J* = 15.7, 7.4 Hz, H-8′), 4.63 (1H, *d*, *J* = 7.5 Hz, H-7), 4.11 (1H, *dd*, *J* = 11.2, 5.3 Hz, H-9a), 4.20 (1H, *dd*, *J* = 11.2, 4.3 Hz,

H-9b), 3.89, 3.87, 3.81 (each 3H, *s*, OMe), 2.32 (1H, *m*, H-8), 2.10-2.20 (2H, *m*, H-9′), 2.06 (3H, $COCH_3$).

**(R)- and (S)-2NMA esters of 9-monoacetate morinol E** Two portions (each 1.0 mg) of 9-monoacetate morinol E were treated with (R)- and (S)-2NMA by the same way as the esterification of morinol B (**2**) which were used (R)- and (S)-MTPA. $^1$H NMR spectral data of (R)-2NMA ester of 9-monoacetate morinol E (400 MHz, δ, ppm, $CDCl_3$): 7.21 (4H, *br d*, *J* = 8.6 Hz, H-2, H-3, H-5 and H-6), 6.92 (2H, *d*, *J* = 8.6 Hz, H-2, H-3, H-5 and H-6), 6.90 (2H, *d*, *J* = 8.6 Hz, H-2, H-3, H-5 and H-6), 6.57-6.84 (6H, *m*, H-2′, H-5′ and H-6′), 6.16 (1H, *d*, *J* = 15.8 Hz, H-7′), 5.95 (1H, *d*, *J* = 15.8 Hz, H-7′), 5.84 (1H, *dt*, *J* = 15.7, 7.4 Hz, H-8′), 5.83 (1H, *d*, *J* = 7.5 Hz, H-7), 5.73 (1H, *dt*, *J* = 15.7, 7.4 Hz, H-8′), 4.95 (1H, *d*, *J* = 7.5 Hz, H-7), 4.24 (1H, *dd*, *J* = 11.0, 5.5 Hz, H-9), 4.10 (1H, *dd*, *J* = 11.2, 4.8 Hz, H-9), 3.96 (2H, *m*, H-9), 3.87, 3.86, 3.85, 3.82, 3.78, 3.70 (each 3H, *s*, OMe), 2.24-2.28 (2H, *m*, H-8), 2.04-2.17 (4H, *m*, H-9′), 1.86, 1.93 (each 3H, $COCH_3$). The $^1$H NMR data of (S)-2NMA ester are the same as those of (R)-2NMA ester.

**Morinol F (6)** Obtained as a colorless oil. $[\alpha]_D^{24}$ +0.8$^0$ ( *c* 0.48; $CHCl_3$ ); IR (KBr) $\nu_{max}$ cm$^{-1}$: 3873, 3739, 3649, 3419, 1618, 1544, 1516, 1467, 1421, 1267, 1178, 1157, 1140, 1023, 826, 759; UV $\lambda_{max}^{CHCl_3}$ nm (logε): 240.2 (sh, 3.81), 271.7 (br, 3.91); The positive HRFABMS: *m/z* 359.1857 (calcd. for $C_{21}H_{27}O_5$, 359.1858); FABMS (*m/z*): 359, 358, 341, 309, 267, 219, 205, 177 (base peak), 151, 137, 136, 135, 121, 91, 77, 55, 41; $^1$H NMR data see Table 3; $^{13}$C NMR and DEPT data see Table 4.

**Morinol G (7)** Obtained as a colorless oil. $[\alpha]_D^{24}$ +1.2$^0$ ( *c* 0.98; $CHCl_3$ ); IR (KBr) $\nu_{max}$ cm$^{-1}$: 3906, 3570, 3433, 1656, 1605, 1544, 1511, 1460, 1264, 1139, 1026, 764; UV $\lambda_{max}^{CHCl_3}$ nm (logε): 240.0 (sh, 3.86), 271.8 (br, 3.94); The positive HRFABMS: *m/z* 389.1963 (calcd. for $C_{22}H_{29}O_6$, 389.1964); FABMS (*m/z*): 389, 388, 339, 323, 267, 219, 205, 177 (base peak), 165, 151, 146, 139, 121, 91, 77, 55, 41; $^1$H NMR data see Table 3; $^{13}$C NMR and DEPT data see Table 4.

**Acetylation of morinol G (7)** 8 mg Morinol G was acetylated by the same way as that of **5**, gave diacetate (2.4 mg) and 9-monoacetate (3.0 mg). $^1$H NMR spectral data of diacetate of morinol G (400 MHz, δ, ppm, $CDCl_3$): 6.78-6.93 (6H, m, Ar-H), 6.23 (1H, *d*, *J* = 15.7 Hz, H-7′), 5.92 (1H, *dt*, *J* = 15.7, 7.4 Hz, H-8′), 5.75 (1H, *d*, *J* = 7.3 Hz, H-7), 4.32 (1H, *dd*, *J* = 11.1, 5.2 Hz, H-9a), 4.14 (1H, *dd*, *J* = 11.1, 4.4 Hz, H-9b), 3.90, 3.89, 3.87, 3.86 (each 3H, *s*, OMe), 2.34 (1H, *m*, H-8), 2.10-2.20 (2H, *m*, H-9′), 2.07 (6H, $COCH_3$); $^1$H NMR spectral data of 9-monoacetate of morinol G (400 MHz, δ, ppm, $CDCl_3$): 6.78-6.92 (6H, m, Ar-H), 6.26 (1H, *d*, *J* = 15.7 Hz, H-7′), 5.95 (1H, *dt*, *J* = 15.7, 7.4 Hz, H-8′), 4.62 (1H, *d*, *J* = 7.3 Hz, H-7), 4.43 (1H, *dd*, *J* = 11.1, 5.3 Hz, H-9a), 4.24 (1H, *dd*, *J* = 11.1, 4.4 Hz, H-9b), 3.90, 3.89, 3.88, 3.87 (each 3H, *s*, OMe), 2.38 (1H, *m*, H-8), 2.10-2.22 (2H, *m*, H-9′), 2.08 (3H, $COCH_3$).

**(R)- and (S)-2NMA esters of 9-monoacetate morinol G** Two portions (each 1.5 mg) of 9-monoacetate morinol E were treated with (R)- and (S)-2NMA by the same way as the esterification of morinol B (**2**) which

were used (R)- and (S)-MTPA. $^1$H NMR spectral data of (R)-2NMA ester of 9-monoacetate morinol G (400 MHz, δ, ppm, $CDCl_3$): 6.44-6.80 (12H, m, Ar-H), 6.18 (1H, *d*, *J* = 15.9 Hz, H-7′), 6.00 (1H, *d*, *J* = 15.9 Hz, H-7′), 5.98 (1H, *dt*, *J* = 15.9, 7.4 Hz, H-8′), 5.96 (1H, *d*, *J* = 7.3 Hz, H-7), 5.94 (1H, *dt*, *J* = 15.9, 7.4 Hz, H-8′), 4.96 (1H, *d*, *J* = 7.3 Hz, H-7), 4.25 (1H, *dd*, *J* = 11.2, 5.2 Hz, H-9), 4.11 (1H, *dd*, *J* = 11.2, 4.4 Hz, H-9), 4.00 (1H, *dd*, *J* = 11.2, 5.4 Hz, H-9), 3.98 (1H, *dd*, *J* = 11.2, 4.3 Hz, H-9), 3.87, 3.86, 3.85, 3.84, 3.83, 3.82, 3.77, 3.71 (each 3H, *s*, OMe), 2.24-2.29 (2H, *m*, H-8), 1.98-2.20 (4H, *m*, H-9′), 2.01, 1.89 ( each 3H, $COCH_3$). The $^1$H NMR data of (S)-2NMA ester are the same as those of (R)-2NMA ester.

**Morinol H (8)** Obtained as a colorless oil. $[\alpha]_D^{24}$ +2.7° ( *c* 0.45; $CHCl_3$ ); IR (KBr) $\nu_{max}$ cm$^{-1}$: 3570, 3401, 2366, 1687, 1656, 1639, 1544, 1511, 1460, 1264, 1139, 1026; UV $\lambda_{max}^{CHCl_3}$ nm (logε): 239.7 (sh, 3.86), 271.8 (br, 3.94); The positive HRFABMS: *m/z* 389.1954 (calcd. for $C_{22}H_{29}O_6$, 389.1964); FABMS (*m/z*): 389, 388, 371, 341, 339, 267, 219, 205, 177 (base peak), 165, 151, 139, 121, 91, 77, 55, 41; $^1$H NMR data see Table 3; $^{13}$C NMR and DEPT data see Table 4.

**Morinol I (9)** Obtained as a colorless oil. $[\alpha]_D^{24}$ +1.6° ( *c* 0.21; $CHCl_3$ ); IR (KBr) $\nu_{max}$ cm$^{-1}$: 3622, 2108, 2042, 1700, 1654, 1623, 1534, 1511, 1475, 1417, 1403, 1264, 1016, 964, 644; UV $\lambda_{max}^{CHCl_3}$ nm (logε): 240.8 (sh, 3.87), 271.9 (br, 3.96); FABMS (+NaI): 393 $[M+Na]^+$, 329, 307, 289, 154, 136, 107, 71; $^1$H NMR data see Table 1; $^{13}$C NMR and DEPT data see Table 2.

**Morinol J (10)** Obtained as a colorless oil. $[\alpha]_D^{24}$ +0.4° ( *c* 0.50; $CHCl_3$ ); IR (KBr) $\nu_{max}$ cm$^{-1}$: 3498, 3434, 2949, 2346, 1719, 1656, 1609, 1561, 1544, 1511, 1460, 1421, 1250, 1158, 1028, 853, 763; UV $\lambda_{max}^{CHCl_3}$ nm (logε): 240.1 (br, 3.82), 265.4 (br, 3.91); The positive HRFABMS: *m/z* 457.2221 (calcd. for $C_{26}H_{33}O_7$, 457.2226); FABMS (*m/z*): 457, 456, 409, 359, 341, 340, 323, 322, 291, 267, 219, 165, 147 (base peak), 121, 91, 77, 55, 41; $^1$H NMR data see Table 1; $^{13}$C NMR and DEPT data see Table 2.

**Morinol K (11)** Obtained as a colorless oil. $[\alpha]_D^{24}$ +3.2° ( *c* 0.74; $CHCl_3$ ); IR (KBr) $\nu_{max}$ cm$^{-1}$: 3570, 3406, 2934, 1719, 1655, 1639, 1608, 1562, 1544, 1511, 1466, 1421, 1250, 1158, 1029, 856, 763; UV $\lambda_{max}^{CHCl_3}$ nm (logε): 240.0 (br, 3.83), 265.5 (br, 3.92); The positive HRFABMS: *m/z* 457.2235 (calcd. for $C_{26}H_{33}O_7$, 457.2226); FABMS (*m/z*): 457, 456, 409, 359, 341, 340, 323, 322, 291, 267, 219, 177 (base peak), 137, 136, 135, 121, 91, 77, 55, 41; $^1$H NMR data see Table 1; $^{13}$C NMR and DEPT data see Table 2.

**Morinol L (12)** Obtained as a colorless oil. $[\alpha]_D^{24}$ +0.8° ( *c* 0.95; $CHCl_3$ ); IR (KBr) $\nu_{max}$ cm$^{-1}$: 3429, 2932, 1719, 1655, 1639, 1608, 1562, 1544, 1511, 1460, 1421, 1250, 1158, 1029, 854; UV $\lambda_{max}^{CHCl_3}$ nm (logε): 240.0 (br, 3.83), 265.5 (br, 3.90); The positive HRFABMS: *m/z* 487.2292 (calcd. for $C_{27}H_{35}O_8$, 487.2332); FABMS (*m/z*): 487, 486, 451, 413, 371, 370, 353, 341, 340, 287, 267, 221, 219, 177 (base peak), 151, 139, 121, 91, 77, 55, 41; $^1$H NMR data see Table 1; $^{13}$C NMR and DEPT data see Table 2.

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