

## A Lignan Glucoside from *Bupleurum scorzonerifolium*

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**Abstract:** A new lignanoside, saikolignanoside A, was isolated from the roots of *Bupleurum scorzonerifolium*. Its structure was determined as 3-methoxy-4-hydroxy-5-[(8'S)-3-methoxy-4-hydroxyphenylpropyl alcohol]-E-cinnamic alcohol-4-O-β-D-glucopyranoside by means of NMR and MS analysis, acid hydrolysis and optical data.

**Keywords:** *Bupleurum scorzonerifolium*, Umbelliferae, lignanoside, saikolignanoside A.

*Bupleurum scorzonerifolium* Willd. has been recorded in the Chinese Pharmacopoeia. Its roots are used as an antiinflammatory and antihepatotoxic agent in Chinese traditional medicine. Although these activities are concerning the saponins from the genus *Bupleurum*<sup>1</sup>, no evidence is available on the activities of its lignan constituents. Most of the reported lignans have been described from the leaves of the genus *Bupleurum*. This paper deals with the isolation and structure identification of a new lignan glucoside from the roots of *Bupleurum scorzonerifolium* Willd..

The roots of *Bupleurum scorzonerifolium* Willd. were collected in Shenmu, Shanxi Province of China and identified by Dr. Chen Hu Biao, Department of Natural medicines, School of Pharmaceutical sciences, Peking University, a voucher specimen is deposited in the herbarium of the Department of Natural Medicines.

7 kg of powdered roots were successively extracted with 95% EtOH and 50% EtOH. The 95% EtOH extract was concentrated under reduced pressure then was extracted with CHCl<sub>3</sub>, EtOAc and *n*-BuOH, respectively. The *n*-BuOH layer were concentrated under reduced pressure yielding powder B<sub>1</sub> (47.0 g). The 50% EtOH extract was concentrated, and extracted with EtOAc and *n*-BuOH, respectively. The *n*-BuOH layer was concentrated to give powder B<sub>2</sub> (160.0 g). 192.0 g of mixed powder from B<sub>1</sub> and B<sub>2</sub> was dissolved in 1 L water, and submitted to a column contained 1 kg of D101 macroporous resin and eluted successively with H<sub>2</sub>O and 80% MeOH, respectively. The MeOH elute was evaporated, the residue was dissolved in MeOH and decolorized by a short Al<sub>2</sub>O<sub>3</sub> column (250 g) eluted with MeOH. The MeOH solution was evaporated and the residue (8.5 g) was subjected to RP-18 column eluted with MeOH: H<sub>2</sub>O = 0:100→100:0. The first fractions were submitted to repeated reverse phase chromatography eluted with MeOH:

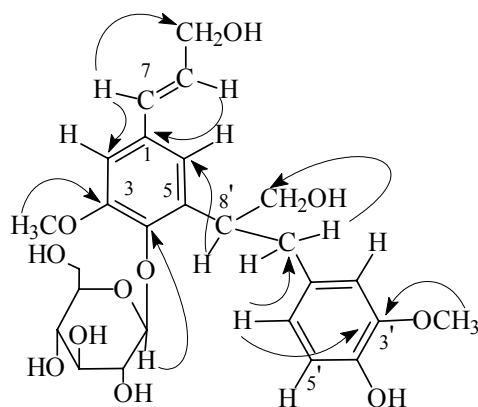
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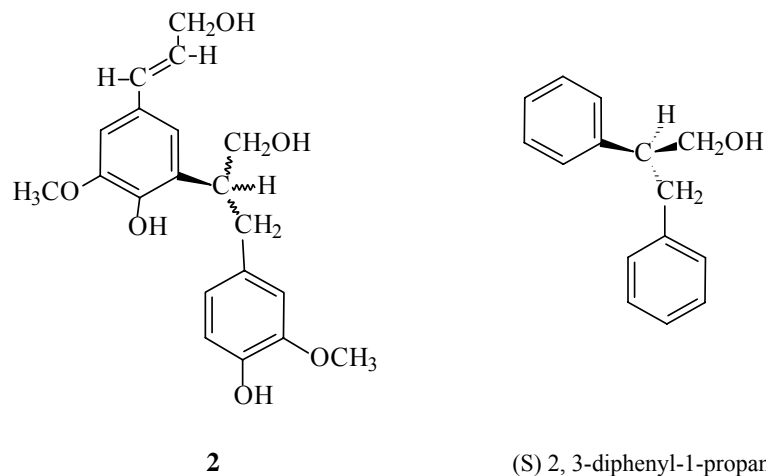
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H<sub>2</sub>O = 20: 80 by HPLC and 15 mg saikolignanose A was obtained.

Compound **1** was isolated as pale-yellow powder, mp. 110-112 °C, and showed positive optical activity  $[\alpha]_D^{23} +32.8$  (c 0.131, MeOH). Negative FAB-MS spectra of this compound gave  $[M-H]^+$  at  $m/z$  521. Its <sup>1</sup>H NMR spectrum showed two doublets at  $\delta$  6.90 (d, 1H, J=2.0 Hz) and  $\delta$  6.89 (d, 1H, J=2.0 Hz) due to a 1,3,4,5-tetrasubstituted aromatic system; two doublets and one double-doublet at  $\delta$  6.63 (d, 1H, J=2.0 Hz),  $\delta$  6.53 (d, 1H, J=7.95 Hz) and  $\delta$  6.44 (dd, 1H, J=7.95, 2.0 Hz) corresponding to a 1,3,4-trisubstituted aromatic system; one doublet and one double-triplet at  $\delta$  6.46 (d, 1H, J=15.0 Hz) and  $\delta$  6.29 (dt, 1H, J=15.0, 5.0 Hz) are attributable to an E double bond. These were further confirmed by its <sup>1</sup>H-<sup>1</sup>H COSY spectrum. The correlations between signals corresponding to protons at  $\delta$  2.89 (dd, 1H) and  $\delta$  2.65 (dd, 1H) (belonging to carbon at  $\delta$  37.26, according to <sup>1</sup>H-<sup>13</sup>C COSY) to a proton at  $\delta$  3.78 (m, 1H, corresponding to carbon at  $\delta$  40.55); protons at  $\delta$  3.57 (m, 1H) and  $\delta$  3.44 (m, 1H) (characteristic of carbon at  $\delta$  64.55) to proton at  $\delta$  3.78 (m, 1H) in <sup>1</sup>H-<sup>1</sup>H COSY, and the signals from the DEPT spectrum showed that the compound possessed the following substructure: -CH<sub>2</sub>-CH-CH<sub>2</sub>-O-. By the analysis of C-H COSY spectrum of **1**, it was clear that the compound consisted of four substructures: two aromatic systems, one double bond system and one -CH<sub>2</sub>-CH-CH<sub>2</sub>-O- system. From the HMBC spectrum, the linkages of the four units were established and the data of <sup>1</sup>H, <sup>13</sup>C NMR and DEPT spectra were also determined (see **Table 1** and **Figure 1**). The signals at  $\delta$  4.65 (d, 1H, J=7.2 Hz) and  $\delta$  103.47 suggested that **1** was a  $\beta$ -glucoside. This was supported by a spin system in its TOCSY spectrum and an ion fragment at  $m/z$  359 corresponding to  $[M-glc]^+$ . Its <sup>1</sup>H, <sup>13</sup>C NMR data were assigned (see **Table 1**) by its DEPT, <sup>1</sup>H-<sup>1</sup>H COSY, <sup>13</sup>C-<sup>1</sup>H COSY and HMBC analysis. The glycosidic linkage was confirmed by HMBC experiments, which showed correlation between the anomeric proton signal,  $\delta$  4.65 (d, 1H, J=7.2 Hz) with C-4 ( $\delta$  142.84) of the aglycone, indicating that the glucose was attached to C-4. The configuration of C-8' of the aglycone was determined based on the analysis of optical rotation.

**Figure 1** HMBC of saikolignanose A (**1**)



**Figure 2** The structure of **2** and (S) 2, 3-diphenyl-1-propanol**Table 1** NMR and DEPT spectral assignments of saikolignanose A (DMSO- $d_6$ ) ( $\delta$  ppm)

|    | $\delta_c$ |                  | $\delta_H$               |     | $\delta_c$ |                 | $\delta_H$         |
|----|------------|------------------|--------------------------|-----|------------|-----------------|--------------------|
| 1  | 133.00     | C                |                          | 1'' | 103.4      | CH              | 4.65 (d, J=7.2Hz)  |
| 2  | 107.97     | CH               | 6.90 (d, J=2.0Hz)        | 2'' | 74.3       | CH              | 3.22 (m)           |
| 3  | 151.60     | C                |                          | 3'' | 76.38      | CH              | 3.20 (m)           |
| 4  | 142.84     | C                |                          | 4'' | 69.56      | CH              | 3.15 (m)           |
| 5  | 137.95     | C                |                          | 5'' | 76.65      | CH              | 3.00 (m)           |
| 6  | 117.74     | CH               | 6.89 (d, J=2.0Hz)        | 6'' | 60.81      | CH <sub>2</sub> | 3.56 (m), 3.44 (m) |
| 7  | 128.57     | CH               | 6.46 (d, J=15.0Hz)       |     |            |                 |                    |
| 8  | 129.84     | CH               | 6.29 (dt, J=15.0, 5.0Hz) |     |            |                 |                    |
| 9  | 61.41      | CH <sub>2</sub>  | 4.09 (m)                 |     |            |                 |                    |
|    | 55.83      | OCH <sub>3</sub> | 3.75 (s)                 |     |            |                 |                    |
| 1' | 131.38     | C                |                          |     |            |                 |                    |
| 2' | 112.67     | CH               | 6.63 (d, J=2.0Hz)        |     |            |                 |                    |
| 3' | 146.95     | C                |                          |     |            |                 |                    |
| 4' | 144.08     | C                |                          |     |            |                 |                    |
| 5' | 114.83     | CH               | 6.53 (d, J=7.9Hz)        |     |            |                 |                    |
| 6' | 120.84     | CH               | 6.44 (dd, J=7.9, 2.0Hz)  |     |            |                 |                    |
| 7' | 37.26      | CH <sub>2</sub>  | 2.89 (dd), 2.65 (dd)     |     |            |                 |                    |
| 8' | 40.55      | CH               | 3.78 (m)                 |     |            |                 |                    |
| 9' | 64.55      | CH <sub>2</sub>  | 3.57 (m), 3.44 (m)       |     |            |                 |                    |
|    | 55.28      | OCH <sub>3</sub> | 3.64 (s)                 |     |            |                 |                    |

After acid hydrolysis of **1** with 1mol/L HCl, the hydrolytic product **2** was obtained, and glucose was detected by comparison with an authentic sample on TLC<sup>2</sup>. **2** showed positive optical activity:  $[\alpha]_{\text{D}}^{25} +20.0$  (c 0.100, CHCl<sub>3</sub>), similar to that of the known compound, S-2,3-diphenyl-1-propanol  $\{[\alpha]_{\text{D}}^{25} +76.3$  (c 5.3, CHCl<sub>3</sub>)<sup>3</sup> (see **Figure 2**). Thus **1** should have 8'S configuration and the structure of **1** is established as 3-methoxy-4-hydroxy-5-[(8'S)-3'-methoxy-4'-hydroxy-phenylpropyl alcohol]-E-cinnamic alcohol-4-O-β-D-glucopyranoside (see **Figure 1**), **1** is a new compound named saikolignanoside A

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