

## First Total Synthesis of 7-O-Geranyl-pseudobaptigenin

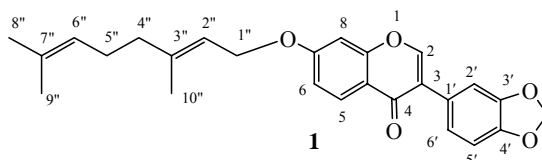
Ya Ping WANG, Liang Xi LI, Jian Jun CHEN, Qing Lian WANG, Yu Lin LI\*

National Laboratory of Applied Organic Chemistry and Institute of Organic Chemistry, Lanzhou University, Lanzhou 730000

**Abstract:** Total synthesis of 7-O-geranyl-pseudobaptigenin is described, the key steps are Grignard reaction and cyclization reaction.

**Keywords:** Synthesis, 7-O-geranyl-pseudobaptigenin, pseudobaptigenin, O-geranylated isoflavone.

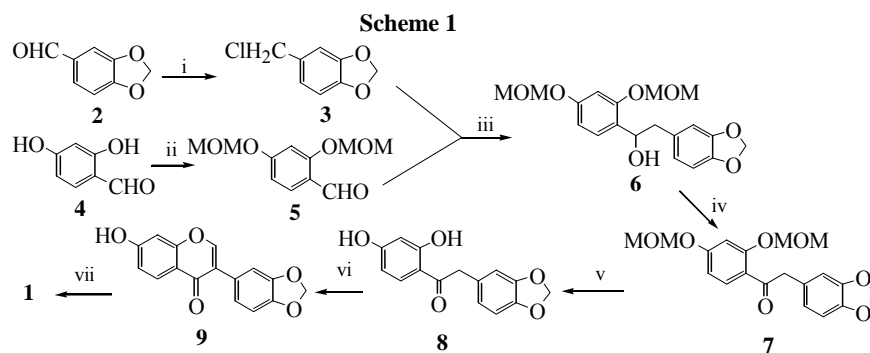
Isoflavones are a class of compounds mainly occurring in species of the *Leguminosae* family. These compounds have received much attention recently due to their interesting biological activities<sup>1</sup>. They have been found to act as the beneficial role in the prevention of hormone based cancers and coronary heart diseases, as well as being potent antioxidant compounds<sup>2</sup>. 7-O-Geranyl-pseudobaptigenin **1** was first isolated from the root bark of *Millettia griffoniana*<sup>3</sup>.



The synthesis of **1** has not been reported, herein we report the first total synthesis of this compound (as shown in **Scheme 1**). This route involved the preparation of deoxybenzoin **8** by Grignard reaction and cyclization of **8** to give isoflavone **9** which reacted with geranyl bromide **10** to give the desired product **1**. This route has the following advantages: (1) It is facile to synthesize the isoflavones which are difficult to get using the previous methods<sup>1,4</sup>; (2) The reagents are cheap and easily available.

Piperonal **2** was reduced with  $\text{KBH}_4$  in methanol in an ice-water bath, then chloridized by  $\text{PCl}_3$  in hexane to give **3** which was treated with magnesium in THF by the initiation of 1,2-dibromo-ethane. Aldehyde **5** (prepared from 2,4-dihydroxy-benzaldehyde **4** by protection with MOMCl) was added to this reaction mixture to give **6**. The oxidation **6** with PCC in dichloromethane afforded ketone **7** and deprotection of **7** gave deoxybenzoin **8**. The cyclization of **8** using  $\text{MeSO}_2\text{Cl}$ -DMF- $\text{BF}_3 \cdot \text{Et}_2\text{O}$  system at  $110 \sim 120^\circ\text{C}$ <sup>5</sup> afforded pseudobaptigenin **9** which is an isoflavone found in many sources<sup>6</sup>. Reaction of **9** with geranyl bromide gave the

desired 7-O-geranyl-pseudobaptigenin **1** in 91% yield, the spectra data of the synthetic **1**<sup>7</sup> are in accordance with that of the natural sample which was reported in the literature<sup>3</sup>.



**Reagents and conditions:** i)  $\text{KBH}_4$ , MeOH,  $0\sim 5^\circ\text{C}$ , 1 h;  $\text{PCl}_3$ , hexane, pyridine, rt, 3 h, 85%; ii) MOMCl,  $\text{K}_2\text{CO}_3$ , acetone, reflux, 1 h, 89%; iii) Mg, THF, rt, 4 h, 45%; iv) PCC, NaOAc,  $\text{CH}_2\text{Cl}_2$ , rt, 1 h, 90%; v) MeOH, THF, 3N HCl, reflux, 1 h, 95%; vi)  $\text{BF}_3 \cdot \text{Et}_2\text{O}$ ,  $\text{MeSO}_2\text{Cl}$ , DMF,  $110\sim 120^\circ\text{C}$ , 6 h, 76%; vii) geranyl bromide,  $\text{K}_2\text{CO}_3$ , dodecyltrimethylammonium bromide, DMF, acetone, reflux, 1.5 h, 91%.

## References and Notes

1. S. Balasubramanian, M. G. Nair, *Synth Commun.*, **2000**, *30*, 469.
2. P. Lewis, K. Wähälä, *Tetrahedron Lett.*, **1998**, *39*, 9559.
3. E. Yankep. Z. T. Fomum, E. Dagne, *Phytochemistry*, **1997**, *46*, 591.
4. M. S. Khanna, O. V. Singh, C. P. Garg, R. P. Kapoor, *J. Chem. Soc., Perkin Trans I*, **1992**, 2565.
5. R. J. Bass, *J. Chem. Soc., Chem. Commun.*, **1976**, 76.
6. D.R. Biggs, G.A. Lane, *Phytochemistry*, **1978**, *17*, 1683.
7. The spectra data of **1**: Fine crystal from methanol, mp  $99\sim 100^\circ\text{C}$ ; IR (KBr  $\text{cm}^{-1}$ ) 1624, 1567, 1440, 1398, 1247, 1039, 1004, 913;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ,  $\delta_{\text{ppm}}$ ): 8.19 (d, 1H,  $J = 8.7\text{Hz}$ , H-5), 7.90 (s, 1H, H-2), 7.10 (s, 1H, H-2'), 7.00 (dd, 2H,  $J = 8.9, 2.0\text{Hz}$ , H-6, 6'), 6.86 (d, 1H,  $J = 9.0\text{Hz}$ , H-5'), 6.85 (d, 1H,  $J = 2.4\text{Hz}$ , H-8), 5.99 (s, 2H,  $-\text{OCH}_2\text{O}-$ ), 5.48 (t, 1H,  $J = 7.0\text{Hz}$ , H-2''), 5.09 (m, 1H, H-6''), 4.64 (d, 1H,  $J = 6.5\text{Hz}$ , H-1''), 2.13 (m, 1H, H-5''), 2.12 (m, 1H, H-4''), 1.77 (s, 3H, H-8''), 1.67 (s, 3H, H-10''), 1.61 (s, 3H, H-9''); EI-MS( $m/z$ ) 418 ( $\text{M}^+$ , 1), 282 (100), 146 (1), 137 (1), 81 (4), 69 (6).

Received 16 October, 2000