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Total Synthesis of the Natural Product-Pinosylvin and its Analog

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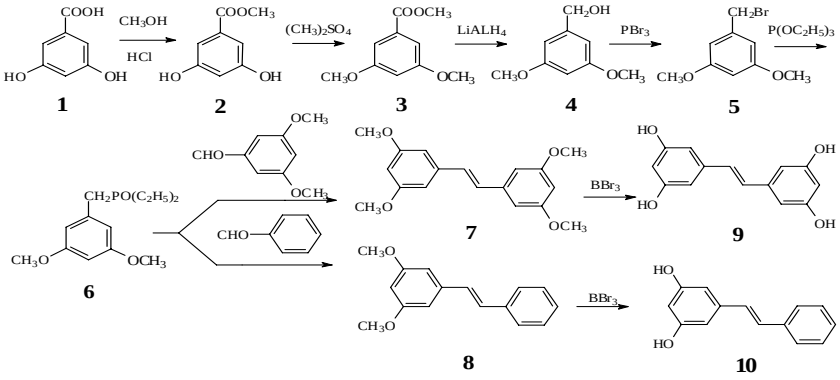
Abstract: We synthesised a natural product (**10**) , isolated from *G.parvifolium* , and its analog. The synthetic product was characterized by elemental analysis and ^{1}H-NMR in comparision with the corresponding natural product.

Keywords: Total synthesis , pinosylvin , analog.

Polyhydroxy stilbenes were proved to have many biological activities[1,2]. We have reported the total synthesis of two natural products-resveratrol (3,5,4'-trihydroxyl stilbene) and isorhapontigenin [3,4] which were first found in a traditional Chinese herb, *G.parvifolium* by M . Lin[5] *et al*. Herein,we want to present the total synthesis of another natural hydroxyl stilbene, pinosylvin (3,5-dihydroxy stilbene,**10**) isolated from this plant and its analog (3,5,3',5'-tetrahydroxy stilbene ,**9**) . In the synthesis of natural hydroxy stilbenes, several kinds of protecting groups have been used according to literature[7,8]. It was reported by Kahitiji Thakkar[6] *et.al*.that [〔tert-butyldimethylsilyl〕oxy] stilbenes were hard to deprotect with increasing substitutions. So they used benzyl groups to protect the phenols with aluminum chloride and N,N-dimethylaniline as the deprotecting agent. We explored methoxy groups as the protecting groups and found the target compounds could be easily obtained with boron tribromide as the deprotective agent. The synthetic route is shown in **scheme 1**. Starting from 3,5-dihydroxybenzoic acid **1**, by 5-step reactions[6], we got compound **6** which reacted with either benzylaldehyde or 3,5-dimethoxy benzylaldehyde using Wittig-Horner reaction to give the precursor **7** and **8**, respectively. Finally, the methoxy groups in **7** and **8** were removed by BBr_3 in the presence of dichloromethane at room temperature under nitrogen. The target products **9** and **10** were purified by column chromatography and characterized by TLC, elemental analysis and ^{1}H-NMR. The spectral data were identical with that of the corresponding natural product .The total yields caculated from **1** are 40%(3,5,3',5'-tetrahydroxy stilbene ,**9**) and 34%(pinosylvin,**10**) , respectively.

Scheme 1 The synthetic route of pinosylvin and its analog



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References and Notes

1. Y. Goda, M. Shibuya, *et al.* , *Chem. Pharm. Bull*., **1987**,*35* (7),2668.
2. E. Mannila, A. Talvitie,*Phytochemistry*, **1992**,*31*(9),3288.
3. Y. B. Feng, L. Wang,*et al* . , *Chinese Chem. Lett.*, **1998**, *9* (11) ,1003.
4. L. Qian, Z.S.Piao,,*et al* . , *Chinese Chem. Lett.*, **2000**,*11*(3),217.
5. J. B. Li , M. Lin, *et al* . ,*Yao Xue Xue Bao.*,**1991**, *26*, 437.
6. K. Thakkar, R. L. Geahlen, *et al.*, *J. Med. Chem*., **1993**, *36*, 2950.
7. R. Bajaj, M. T. Gill *et al*., *Rev. Latinoamer. Quim*., **1987**, *18*, 79.
8. E. Reimann, *Tetrahedron Lett.*, **1970**, 4051.
9. For compound **7**, mp 136-138℃; ^{1}H-NMR 300MHz,$CDCl_3$ δ ppm : 7.015 (s,2H, α, β-H), 6.668 (d,4H,J=2.1Hz,2,6,2',6'-H), 6.404 (t,2H,J=2.1Hz,4,4'-H), 3.834 (s,12H, OCH_3). For compound **8**,mp 53-54 ℃ ; ^{1}H-NMR 300MHz,$CDCl_3$ δ ppm :7.517 (m,2H,2',6'-H), 7.366 (m,2H,3',5'-H), 7.268 (m,1H,4'-H), 6.685 (d,2H,J=2.4Hz,2,6- H), 6.409 (t,1H,J=2.4Hz,4-H), 3.840 (s,6H, OCH_3), 7.106,7.035 each 1H (d,J=16.2Hz, α, β -H). For compound **9** mp 200℃dec; ^{1}H-NMR,300MHz, DMSO-d_6 δ ppm: 6.538 (d, 4H, J=2.1Hz,2,6,2',6'-H), 6.279 (t, 2H,J =2.1Hz,4,4'-H), 6.919 (s, 2H, α, β -H), 8.272 (s,D_2O exchangeable); elemental analysis: $C_{14}H_{12}O_4 \cdot 0.5\ H_2O$, calcd. C: 66.40%, H 5.17%, found C 66.51%, H 5.17%. its spectrum data and TLC are identical with the corresponding natural product. For compound **10**, mp 156-158℃; ^{1}H-NMR,300MHz, CD_3COCD_3-d_6 δ ppm: 7.532 (brd,2H,J=7.5Hz,2',6'-H), 7.326 (brt,2H, J=7.5Hz,3',5'-H), 7.220 (brt,1H,J=7.5Hz,4'-H), 6.548 (d,2H,J=1.8Hz,2,6-H), 6.263 (t,1H,J=1.8Hz, 4-H), 7.085, 7.023 each 1H (d,J=16.5Hz α, β -H); 8.882 (s,D_2O exchangeable); elemental analysis : $C_{14}H_{12}O_2$, calcd. C: 79.23%, H 5.70%, found C 79.07%, H 5.72%. Its sp ectrum data and TLC are identical with the corresponding natural product.

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