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Enantioselective Total Synthesis of Four Styrylpyrone Derivatives

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Abstract: The first enantioselective total synthesis of 5-acetoxygoniothalamin **1** and 5-acetoxyisogoniothalamin oxide **2** was achieved through the Sharpless kinetic resolution of racemic secondary 2- furylmethanol **5** and the Mitsunobu reaction. At the same time we developed a short synthetic route for 6R-(+)-goniothalamin **3** and (6R, 7R, 8R)-(+)-goniothalamin oxide **4**. And according to this route the configuration of 5-acetoxygoniothalamin **1** was confirmed as (5S, 6S).

Keywords: Enantioselective, 5-acetoxygoniothalamin, 5-acetoxyisogoniothalamin oxide, 6R-(+)-goniothalamin, (6R, 7R, 8R)-(+)-goniothalamin oxide.

Most of 6-substitute 5, 6-dihydro-2H-pyran-2-ones exhibit significant bioactivities. 5-acetoxygoniothalamin **1** was isolated from the roots of *Goniothalamus uvaroides*[1]. 5-acetoxyisogoniothalamin oxide **2** was isolated from the stem bark of *G.sesquipedalis*[2]. 6R-Goniothalamin **3** and 6R, 7R, 8R-(+)-goniothalamin oxide **4** have been isolated from *Goniothalamus macrophyllus* as the active embryotoxic and teratogenic components[3-5]. The configuration of goniothalamin oxide **4** is (6R, 7R, 8R) rather than the (6S, 7R, 8R) assignment, which was established by chemical transformations and single crystal X-ray crystallography as (6R, 7R, 8R)[5]. Now we report the first enantioselective synthesis of 5-acetoxygoniothalamin **1** and 5-acetoxyisogoniothalamin oxide **2** based on the Sharpless kinetic resolution of racemic secondary 2-furylmethanol **5**[6] and the Mitsunobu reaction[7]. And according to this route the configuration of 5-acetoxygoniothalamin **1** was confirmed as (5S, 6S). At the same time we successfully synthesized 6R-(+)-goniothalamin **3** and (6R, 7R, 8R)-(+)-goniothalamin oxide **4** through a shortly synthetic route. According to this route alcohol **6** was deoxygenated by successive methanesulfonylation and lithium aluminum hydride reduction of mesylate to afford the dihydropyran **8**[8], which is desirable to improve our synthetic route. Our spectrum data agree with those previously reported[1-5]. The synthetic strategy is shown in **Scheme 1**. This route provides rapid and enantioselective access to α, β-unsaturated δ-lactones that are useful synthons for the synthesis of natural product.

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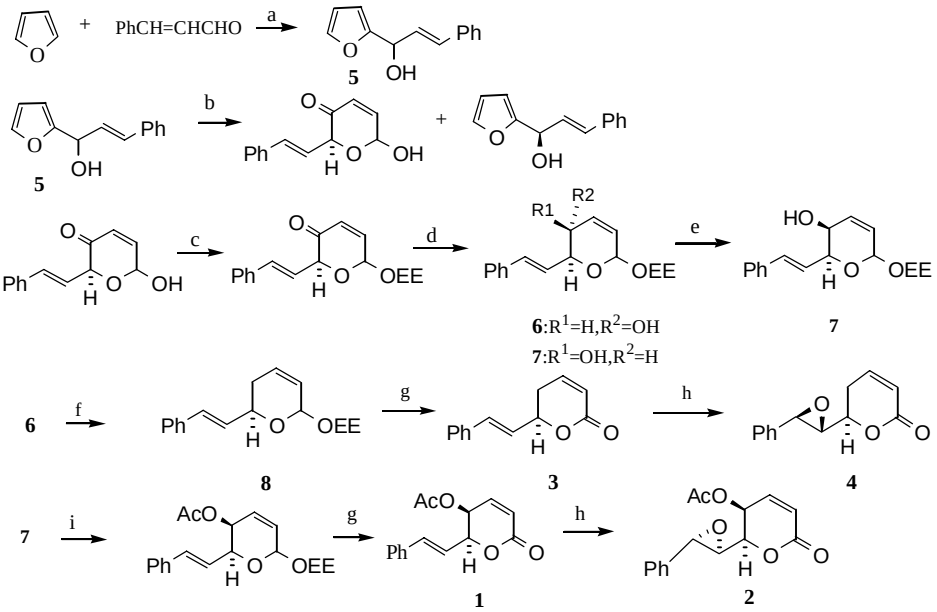
Scheme 1



Reagents and conditions

a) BuLi, THF, -78°C; b) L-(+)-DIPT, $Ti(O\text{-}^{i}Pr)_4$, TBHP, CH_2Cl_2, -25°C; c) ethyl vinyl ether, PPTS, CH_2Cl_2, RT; d) $NaBH_4$, $CeCl_3 \cdot 7H_2O$, MeOH, -30--40°C; e) DEAD, PPh_3, *p*-$NO_2C_6H_5COOH$, THF; then K_2CO_3, MeOH; f) i. Et_3N, DMAP, CH_3SO_2Cl, 0°C; ii. $LiAlH_4$, 50°C; g) CrO_3, HOAc; h) m-CPBA, CH_2Cl_2. i) Ac_2O, py, DMAP, RT.

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8. Compound **8:** $[\ ]_D^{25}$ +93 (c 0.4, $CHCl_3$), IR (KBr, cm^{-1}): 1680, 1640; *m/z* (EI) 229 (M^+-45), 131, 115, 103; ^{1}HNMR (400MHz, $CDCl_3$) 1.21 and 1.24 (each t, 3H, *J*=7.2Hz), 1.41 and 1.43 (each d, 3H, *J*=4.8 Hz), 2.12-2.25 (m, 2H), 3.53-3.74 (m, 2H), 4.58 (m, 1H), 4.96 and 5.03 (each q, 1H, *J*=5.6 Hz, OCHMe), 5.27 and 5.37 (each br s , 1H), 5.75 and 5.81 (m, 1H), 6.09 (m, 1H), 6.27 (dd, 1H, *J*=16.2 and 5.9 Hz), 6.65 (d, 1H, *J* =16.2 Hz) and 7.25-7.43 (m, 5H).

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