

Preparation of *E*- and *Z*- α -Arylidene- γ -butyrolactones from *Z*- α -Stannylmethylene- γ -butyrolactones: Stereoselective Synthesis of (\pm)-Savinin and (\pm)-Gadain

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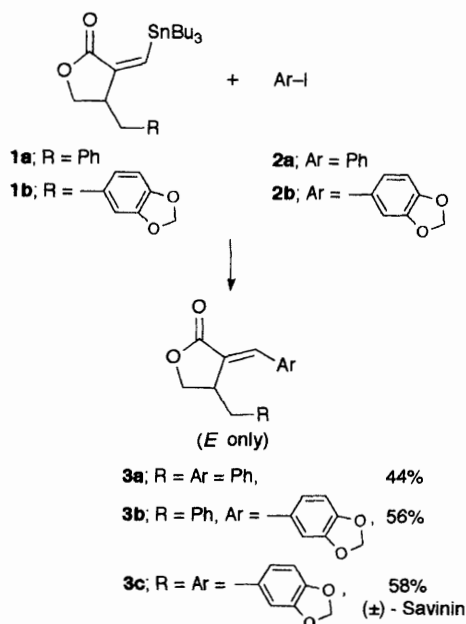
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E- α -Arylidene- γ -butyrolactones were prepared by the radical addition–elimination reaction of *Z*- α -stannylmethylene- γ -butyrolactones, whereas the palladium(0) catalysed cross-coupling reaction of the same substrates afforded *Z*- α -arylidene- γ -butyrolactones.

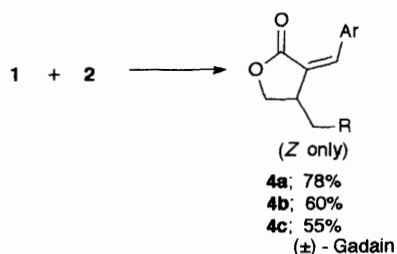
Recently we reported a convenient method for the synthesis of *Z*- α -stannylmethylene- γ -butyrolactones which were easily transformed into α -methylene- γ -butyrolactones upon destannylation.¹ Vinylstannanes may serve as substrates in more useful transformations.^{2–4} We now report substitution reactions of *Z*- α -stannylmethylene- γ -butyrolactones with aryl halides which result in the formation of α -arylidene- γ -butyrolactones. Two methods were considered for the elaboration of a stannylmethylene group into an arylidene group: aryl radical addition–stannyl radical elimination and palladium-catalysed cross-coupling reaction with aryl halides. The chemistry of α -stannylmethylenelactones is not well known yet, and the above reactions may lead to alternative synthesis of lignan lactones.⁵

The *Z*- α -stannylmethylene- γ -butyrolactone **1** substrates were prepared from appropriate allylic propiolates in 60–80% yields by slow addition of tributylstannane solution containing 0.15 equiv. of azoisobutyronitrile (AIBN).¹ A solution of **1** (2.0 mmol) and the aryl halide **2** (1.0 mmol) in benzene (3.0 ml) was heated under reflux and a solution of tributylstannane (1.0 mmol) and AIBN (0.1 mmol) in benzene (3.0 ml) was added by a syringe pump over 5 h. Products were isolated in 44–58% yields along with recovered substrates.⁶ *E*- α -Arylidene products **3** were obtained exclusively. 3,4-Methylene-dioxyphenyl iodide **2b** participated in the substitution reaction, thus paving the way for the synthesis of (\pm)-savinin **3c**.⁶

Z- α -Arylidene- γ -butyrolactones **4** were synthesized via palladium-catalysed arylation. A solution of the lactone **1a**

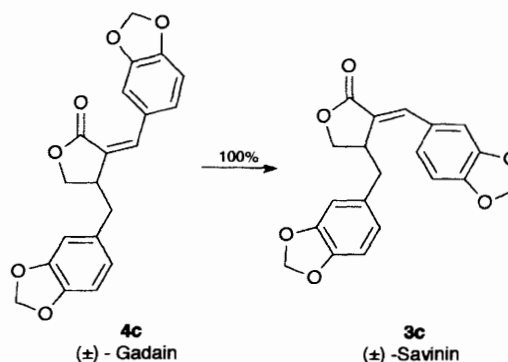


Scheme 1 Reagents and conditions: Bu_3SnH , AIBN (cat.), slow addition (5 h), refluxing C_6H_6



Scheme 2 Reagents and conditions: $\text{Pd}(\text{dba})_2$, refluxing toluene (12 h) for **4a**; $\text{Pd}(\text{dba})_2$, DMF (80 °C, 16 h), Bu^n_4NI for **4b,c**; **4a-c**, **a-c** as for **3**

(1.0 mmol), iodobenzene **2a** (1.0 mmol) and a catalytic amount of bis(dibenzylideneacetone)palladium [$\text{Pd}(\text{dba})_2$; 5 mol%] in toluene (3.0 ml) was heated under reflux to give *Z*- α -benzylidene- β -benzyl- γ -butyrolactone **4a** in 78% yield. 3,4-Methylenedioxyphenyl iodide **2b** did not participate in the palladium(0)-catalysed substitution reaction in toluene, but in dimethylformamide (DMF) with a phase-transfer catalyst the reaction proceeded in reasonable yield.⁷ (±)-Gadain **4c** was



Scheme 3 Reagents and conditions: Bu_3SnH , AIBN (cat.), refluxing C_6H_6 , 1 h

synthesized in this way in 55% yield.⁸ The *Z*- α -arylidene- γ -butyrolactones **4** were quantitatively isomerised into the corresponding *E*-isomers **3** under the radical generating conditions. For example, the treatment of (±)-gadain **4c** (1.0 mmol) with tributylstannane (1.0 mmol) in the presence of a catalytic amount of AIBN in boiling benzene (3.0 ml) for 1 h gave (±)-savinin **3c** quantitatively.[†]

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[†] In ^1H NMR spectra, the vinylic hydrogen resonances of the *Z*- α -arylidene- γ -butyrolactones always appear downfield relative to the corresponding signal in the *E*-isomers: for example, δ 7.72 for gadain and δ 7.50 for savinin.