

## Synthesis of Butyrolactone Lignans

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**Keywords:** Matairesinol, Arctigenin, C-H Insertion Reaction, Butyrolactone Lignans, Horner-Wadsworth-Emmons Reaction

Matairesinol and arctigenin (Fig. 1), which were butyrolactone-type lignans, are found in seeds such as flax and sesame, and vegetables such as wheat, pumpkin, and burdock. They have been reported physiological activities such as antioxidant, anticancer, and anti-HIV. Because of their potent anticancer activity against various cancer cell lines such as pancreatic, breast, lung, and bladder cancers, matairesinol and arctigenin were attracted attentions. And they may be expected to apply to anticancer therapy. On the other hand, rhodium (II) catalyzed C-H insertion of  $\alpha$ -diazo- $\beta$ -keto compounds was useful to five-membered ring construction. In this study, we report the convenient synthesis of matairesinol and arctigenin, and their analogues using the C-H insertion reaction as key reaction.

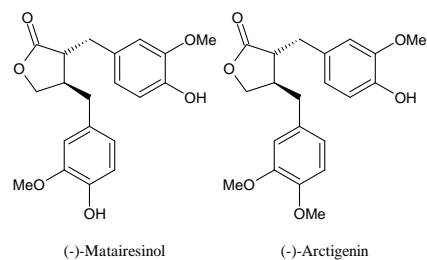
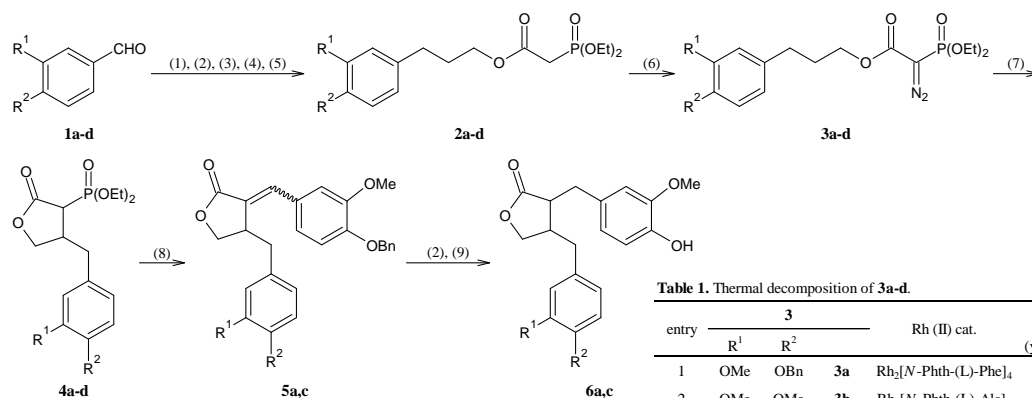


Fig. 1. (-)-Matairesinol and (-)-Arctigenin

The phosphonoacetates **2a-d** were prepared from benzaldehydes **1a-d** with Horner-Wadsworth-Emmons (HWE) reaction, hydrogenation, reduction, esterification, and Arbuzov reaction in 74-86% yields. Diazo transfer reaction of **2a-d** with *p*-toluenesulfonyl azide gave diazo compounds **3a-d** in 40-54% yields. Thermal decomposition of **3a-d** in the presence of rhodium (II) catalysts gave  $\gamma$ -butyrolactones **4a-d** in 33-38% yields (Table 1). The reaction of **4a,c** with **1a** gave the HWE reaction products **5a,c** in 25-46% yields. Hydrogenation and hydrogenolysis of **5a,c** gave matairesinol **6a** and its analogue **6c** in 7% and 15% yields, respectively (Scheme 1).



Scheme 1. Synthesis of 6.

**Reagents and conditions:** (1) NaH, (EtO)<sub>2</sub>P(O)CH<sub>2</sub>CO<sub>2</sub>Et, THF, r.t.; (2) PtO<sub>2</sub>, H<sub>2</sub>, benzene, r.t.; (3) LiAlH<sub>4</sub>, THF, reflux; (4) ClCH<sub>2</sub>COCl, Et<sub>3</sub>N, CH<sub>2</sub>Cl<sub>2</sub>, r.t.; (5) (EtO)<sub>2</sub>P, 150 °C; (6) NaH, TosN<sub>3</sub>, THF, r.t.; (7) Rh(II) cat., solv., Temp.; (8) Base, **1a**, THF, r.t.; (9) Pd/C, H<sub>2</sub>, EtOH, reflux

Table 1. Thermal decomposition of **3a-d**.

entry	<b>3</b>		Rh (II) cat.	Product (yield, %) <sup>1)</sup>
	R <sup>1</sup>	R <sup>2</sup>		
1	OMe	OBn	Rh <sub>2</sub> [N-Phth-(L)-Phe] <sub>4</sub>	<b>4a</b> (38)
2	OMe	OMe	Rh <sub>2</sub> [N-Phth-(L)-Ala] <sub>4</sub>	<b>4b</b> (36)
3	OBn	OMe	Rh <sub>2</sub> [N-Phth-(L)-Ala] <sub>4</sub>	<b>4c</b> (35)
4	OBn	OBn	Rh <sub>2</sub> [N-Phth-(L)-Ala] <sub>4</sub>	<b>4d</b> (33)

1) Isolated yield.