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# Phosphorus, Sulfur, and Silicon and the Related Elements

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## Asymmetric Synthesis of Eucomol via Enantioselective Oxidation of Enol Phosphate

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### ASYMMETRIC SYNTHESIS OF EUCOMOL VIA ENANTIOSELECTIVE OXIDATION OF ENOL PHOSPHATE

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#### **GRAPHICAL ABSTRACT**



ligand (DHQD)<sub>2</sub>-PHAL, K<sub>3</sub>Fe(CN)<sub>6</sub>, K<sub>2</sub>CO<sub>3</sub>, OsO<sub>4</sub>, CH<sub>3</sub>SO<sub>2</sub>NH<sub>2</sub> reaction time 24h, 0°C

Abstract Stereoselective synthesis of a few derivatives of the homoisoflavanone class of

natural products is described.

Keywords Eucomol; eucomin; enol phosphate; enantioselective oxidation

#### INTRODUCTION

Natural products, homoisoflavones or homoisoflavanones, were discovered by Bohler and Tamm – the chemist from University in Basel, who isolated two members of this class: (-)-(S)- eucomol and eucomin from the bulbs of *Eucomis bicolor* BAK (Liliaceae).<sup>1</sup>

The only one enantioselective synthesis of 5,7-*O*-dimethyleucomol **1**, was realized by Davis<sup>2</sup> and co-workers in 1990, using own chiral reagent, (-)-[(8,8-dimethoxycamphoryl)sulfonyl] oxaziridine, for asymmetric  $\alpha$ -hydroxylation of the lithium enolate of 5,7-dimethoxy-3-(4-methoxybenzyl)chroman-4-one.

As a part of our interest in the application of organophosphorus derivatives in the synthesis of functionalized, enantiomerically enriched, cyclic compounds, we have elaborated upon a methodology based on another type of enol derivative – readily available enol phosphates – for the synthesis of  $\alpha$ -hydroxy carbonyl compounds.<sup>3</sup> Herein, we present our studies on the asymmetric synthesis of the title compound, namely 5,7-*O*-dimethyleucomol **1**.

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#### **RESULTS AND DISCUSSION**

Our approach to the synthesis of the enantiomeric 5,7-O-dimethyleucomol 1 was based on the asymmetric oxidation of the corresponding enol phosphate 2, using organic catalyst – chiral oxidant dioxirane, generated *in situ* from fructose derivative 3, and also chiral Sharpless' reagent.<sup>4</sup> This enol phosphate 2 was prepared by the standard procedure, from the dihydroeucomin 4 (derived from 5,7-O-dimethyleucomin 5 by hydrogenation) and diethylphosphorochloridate (Scheme 1).



Several methods of the synthesis of the key compound -5,7-O-dimethyleucomin **5** and its analogs have been described in literature.<sup>5</sup> We decided to explore the procedure, reported for the synthesis of its analogs by Basavaiah<sup>6</sup> and co-workers. This procedure involved the conversion of adduct **6** into acid **7** via two step transformation. Ring closure in **7** with trifluoroacetic anhydride gave the final product -5,7-O-dimethyleucomin **5**. Next, hydrogenation of **5** and subsequent phosphorylation reaction afforded the desired enol phosphate **2** (Scheme 1).

The asymmetric epoxidation of enol phosphate 2 using the chiral dioxirane generated from Oxone (2KHSO<sub>5</sub>•KHSO<sub>4</sub>•K<sub>2</sub>SO<sub>4</sub>) and fructose ketone 3 was carried out under catalytic conditions and afforded a new epoxide 8 with high enantiomeric excess, albeit in low yield (15%) (Scheme 2). The structure of the epoxide 8 was characterized by mass spectrometry and NMR spectroscopy. The characteristic chemical shift of the 2-H epoxide proton in 8 ( $\delta_{\rm H} = 5.14$  ppm) corresponds to the literature reports.<sup>7,8</sup>

Thus, we used another approach to the synthesis of enantiomeric eucomols. This oxidation reaction of enol phosphate 2 was performed according to described Sharpless' procedure,<sup>4</sup> elaborated for catalytic asymmetric dihydroxylation reactions of tetrasubstituted cyclic enol derivatives (Scheme 3).

The desired 5,7-O-dimethyleucomol **1** was obtained in good yield but with low enantiomeric excess of 18%.

Further investigation of the influence of substituents at phosphorus and the choice of the asymmetric oxidation conditions continues.



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