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Yeast-Mediated Regio- and Stereoselective Reduction of Dialkyl 2,4-Dioxy-4-substituted Butanephosphonates

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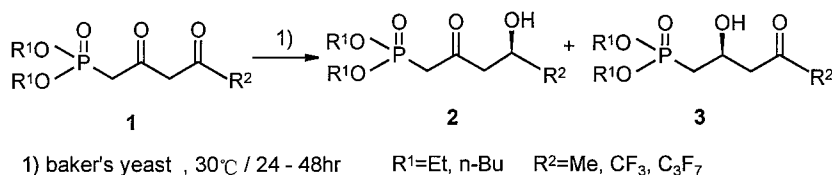
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YEAST-MEDIATED REGIO- AND STEREOSELECTIVE REDUCTION OF DIALKYL 2,4-DIOXY-4-SUBSTITUTED BUTANEPHOSPHONATES

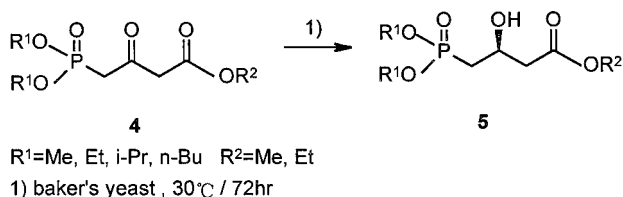
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A series of phosphorus-based carbonyl compounds, namely, dialkyl 2,4-dioxy-4-substituted butane phosphonates (**1**), was prepared by reaction of carbanion resulted from 2-methyl-2-oxoethane phosphonate with substituted acetates. Bioreduction of **1** by baker's yeast at 30°C for 24–48 h usually offered an isomeric mixture; when R¹ is methyl, the isomeric mixture of **2** and **3** in 45 and 24 yield as well as 92% and 80% ee value respectively. It is interesting to note that when R² is CF₃ or C₃F₇, a regio- and stereoselective reduction was observed. Thus, only **2** was obtained in 54–67% yield and 90–94% ee value.



SCHEME 1



SCHEME 2

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On the other hand, dialkyl 2,4-dioxy-4-alkoxy-butanephosphonates (**4**) constitute another class of diketo-phosphonates, in which carboxylate and phosphonate groups are located in the same molecule and separated by a carbonyl group. Our experimental results demonstrated that upon this bio-reduction, (R)-hydroxy derivatives (**5**) were isolated in mediate, 46–77% chemical yield and 50–85% ee value.