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The Synthesis of 1-Hydroxy Phosphonates of High Enantiomeric Excess Using Sequential Asymmetric Reactions: Titanium Alkoxide Catalyzed P--C Bond Formation and Kinetic Resolution

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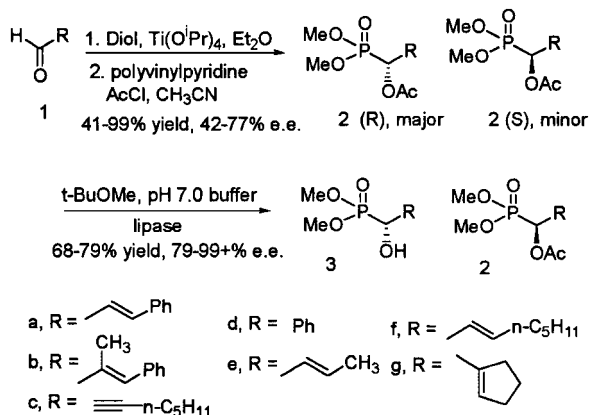
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THE SYNTHESIS OF 1-HYDROXY PHOSPHONATES OF HIGH ENANTIOMERIC EXCESS USING SEQUENTIAL ASYMMETRIC REACTIONS: TITANIUM ALKOXIDE CATALYZED P–C BOND FORMATION AND KINETIC RESOLUTION

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Titanium alkoxyde-catalyzed asymmetric phosphonylation of aldehydes yields hydroxy phosphonates in moderate to good enantiomeric excess (~70%). The hydroxy phosphonates were acetylated and the acetates were subjected to an enzyme-catalyzed kinetic resolution. The non-racemic acetates **2** (*R* major) were hydrolyzed with an *R*-selective lipase, resulting predominantly in the hydrolysis of the *R* isomer (at 85% conv.) to give the alcohols **3** with high enantiomeric excess. Alternatively, hydrolysis of the minor enantiomer (*S* acetate to approx. 20% conv.) left the *R* acetate with improved enantiomeric excess (>90%).



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