ENANTIOSELECTIVE SYNTHESIS OF PROPARGYL ALCOHOLS WITH DIYNES UNDER CARREIRA CONDITIONS

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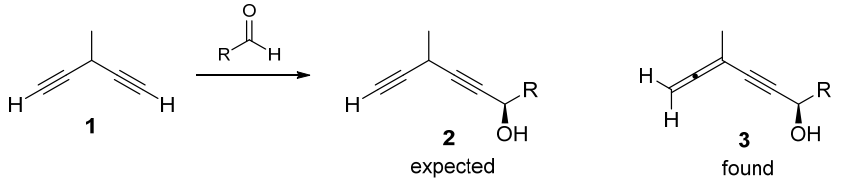
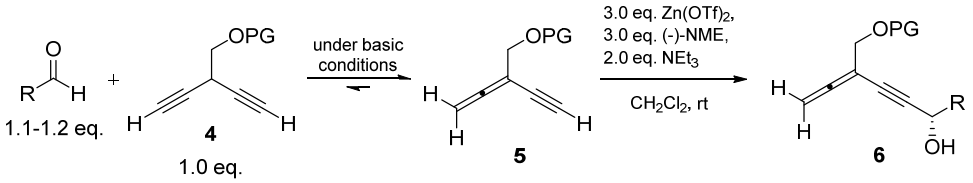
In the year 2000, Carreira and coworkers described an elegant method for the synthesis of enantioselective propargyl alcohols.[1, 2, 3, 4, 5, 6]

In the course of a total synthesis, we initially attempted to synthesize propargyl alcohol **2** from 3-Methylpenta-1,4-diyne **1** (scheme 1).



Scheme 1. Primary synthesis of propargyl alcohol **2**.

Unexpectedly we found compound **3**, so we tested the reactions under Carreira conditions with 1,4-pentadiynes **4** as starting materials using (1R,2S)-(-)-N-Methylephedrine ((-)-NME) as chiral ligand in combination with zinc trifluoro-methanesulfonate and triethylamine. The chiral ligand (-)-NME affords the alcohols with (*S*)-configuration.[7] Under basic conditions the pentadiynes **4** isomerised to an allene-yn **5** which was converted to the propargylic alcohols **6**. Best yields (70 %) and enantiomeric ratios (> 90 % : < 10 %) were realized with 3.0 equiv. $Zn(OTf)_2$ and (-)-NME and 2.0 equiv. NEt_3 at room temperature.



Scheme 2. General reaction with pentadiynes **4** and aldehyde under Carreira conditions.

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