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Chemoselective Reduction by $Cp_2Zr(H)Cl$ (Schwartz's Reagent)

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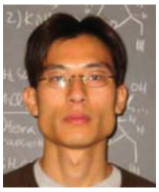
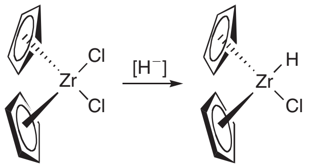


Heedong Yun received a B.S. in 1999 from Seoul National University. He obtained an M.A. from Columbia University in 2003 and currently he is pursuing a Ph.D. under the guidance of Samuel Danishefsky on the total synthesis of biologically active marine natural products.

Background and Preparation

Since the preparation of the first organochlorobis(cyclopentadienyl) zirconium complex by Wailes and Weigold in 1970,[1] organozirconocenes have emerged as one of the most useful classes of transition metal derivatives in organic synthesis. The wide range of transformations mediated by zirconocenes and the easy preparation of such species have contributed to the broad appeal of such reagents. In particular, Schwartz and coworkers pioneered the use of hydrozirconation for the functionalization of organic compounds.[2] $Cp_2Zr(H)Cl$ (Scheme 1) was first prepared by Wailes et al.[1] by reduction of Cp_2ZrCl_2 with $LiAlH_4$ in tetrahydrofuran[3] as well as by magnesium metal reduction. This reagent is also prepared by reduction with $LiAl(OBu^t)_3H$[4] and Red-Al.[5] Much of the development of the chemistry of organozirconocenes has focussed on carbon–carbon and carbon–heteroatom bond formations.[6] Recently, however, it has been recognized that the title reagent is also especially useful for effecting chemoselective reductions of carbonyl groups and other compounds.

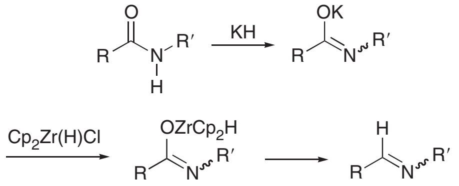


Scheme 1.

Applications

Reduction of 2° Amides or Lactams to Imines

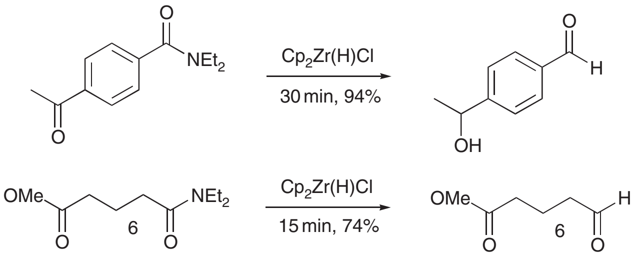
Zirconium(IV) salts of 2° amides or lactams were transformed by Schwartz's reagent to *N*-substituted imines (Scheme 2).[7] The method represents controlled reduction of amides and lactams to the corresponding imines, a transformation that is otherwise very difficult to achieve because imines are reduced more rapidly than carboxamides by most metal hydride reagents.



Scheme 2.

Reduction of 3° Amides to Aldehydes

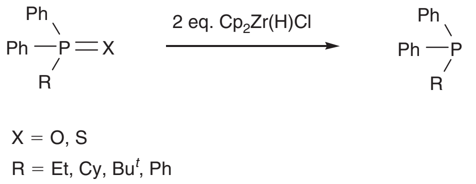
A convenient procedure for the conversion of 3° amides to aldehydes under very mild conditions was introduced (Scheme 3).[8] The ketone functionality also present in the molecule is reduced to an alcohol together with amide reduction. Of additional particular interest is that in the presence of an ester functionality, a 3° amide can be reduced selectively to the corresponding aldehyde in very good yield.



Scheme 3.

Reduction of Phosphine Oxides or Sulfides to Phosphines

Reduction of phosphine oxides or sulfides can be achieved using several reagents.[9] The most popular reductants are silanes which can be used generally in the presence of other functionalities. However the other reducing agents are not so selective and many functionalities are sensitive to reduction by them. Schwartz's reagent selectively reduced a variety of functionalized phosphine oxides or sulfides efficiently (Scheme 4).[10]



Scheme 4.

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(*b*) Schwartz's reagent is commercially available from various suppliers, for example Aldrich catalog number 22367-0.

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