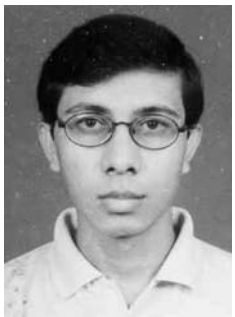
SYNLETT
Spotlight 64

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Zirconium Tetrachloride

Compiled by Utpal Bora



Utpal Bora received his MSc degree (Chemistry) in 1999 from Gauhati University, Assam, India. He then joined Dr R. C. Boruah's research group in the Medicinal Chemistry Division at the Regional Research Laboratory (CSIR), Jorhat, Assam, India to pursue his PhD. His research interests include steroidal ring-D manipulation, new synthetic strategies, and biotransformation reactions.

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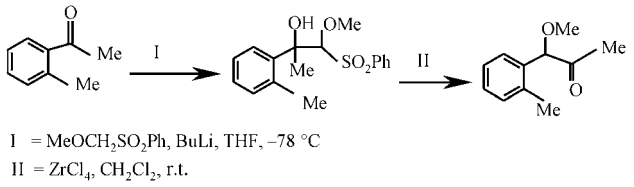
The use of transition metal salts in organic synthesis is an emerging area of research. Due to their low toxicity (LD_{50} [$ZrCl_4$, oral rat] = 1688 $mgKg^{-1}$),[1] low cost, ease of handling, and high catalytic activity, the Zr(IV) compounds are potential green catalysts. $ZrCl_4$ is a relatively weak Lewis acid,[2] which finds uses in Friedal–Crafts reaction,[3] Diels–Alder reactions,[4] asymmetric Diels–Alder reaction,[5] [2+2]-adduct formation,[6] and intramolecular cyclization.[7] The application of $ZrCl_4$ in organic reactions is gaining renewed interests.

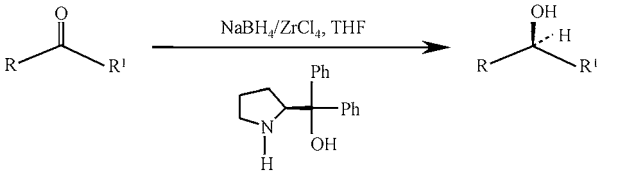
Zirconium tetrachloride may be prepared by chlorination of heated zirconium, zirconium carbide, or a mixture of ZrO_2 and charcoal.[8]

Abstract

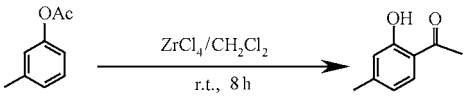
(A) $ZrCl_4$ facilitates a high yielding homologation of ketones into α-methoxy ketones[9] via intermediate sulfone adducts. This procedure allows the sulfone mediated homologation methodology to be applied to monocyclic and acyclic ketones.



(B) $ZrCl_4/NaBH_4$ reduces[10] various functional groups including carbonyls, olefins, imines, and nitriles. The above reducing system along with a chiral amino alcohol have been successfully applied to the enantioselective reduction of oxime ethers.[11] $ZrCl_4$ in the presence of $NaBH_4$ and (*S*)(–)-α,α-diphenyl prolinol catalyzed the enantioselective reduction of prochiral ketones with moderate to high enantiomeric excess.[12]



(C) $ZrCl_4$ is an excellent mediator of the Fries reaction[13] and it transforms 6-methoxytetralins into 8-methoxytetralins.[14] The Fries rearrangement occurs at ambient temperature and is highly selective with preferential migration towards the least sterically encumbered adjacent carbon centre. Use of ultrasound in this reaction is often beneficial.



Synlett 2003, No. 7, Print: 02 06 2003.
Art Id.1437-2096,E;2003,0,07,1073,1074,ftx,en;V06603ST.pdf.
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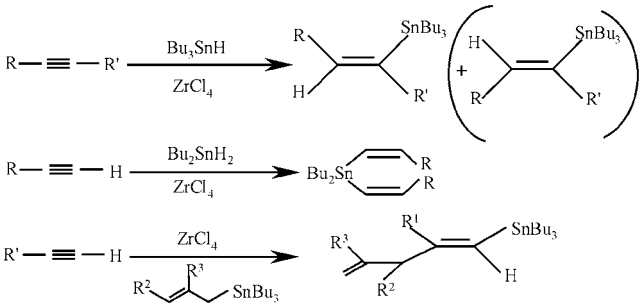
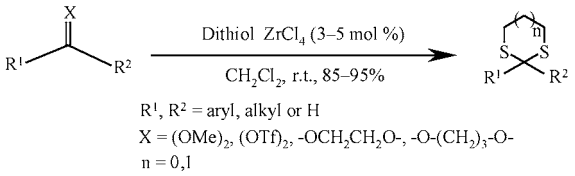
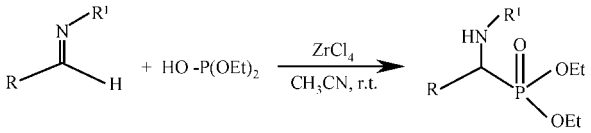
(D) $ZrCl_4$ catalyzed the hydrostannation[15] of acetylenes by tributyltin hydride to produce the *cis*-vinylstannanes by regio- and stereoselective *anti*-hydrostannation. The hydrostannation of acetylene using dibutyltin dihydride is also catalyzed by $ZrCl_4$ to give the stereodefined *Z-Z* divinyltin derivatives by an *anti*-hydrostannation pathway.[15] This reaction at 0 °C gave better yields and stereoselectivity than the reaction at room temperature. The *trans*-allylstannylation of simple acetylenes is also catalyzed by $ZrCl_4$ to produce alkenylstannanes[16] in a regio- and stereoselective manner.



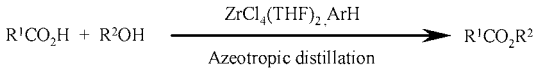
(E) $ZrCl_4$ is an effective catalyst for highly chemoselective transthioacetalization of acetals[17] under mild reaction condition. High rates of reaction, mild reaction conditions, high chemoselectivity, easy work-up and high yields of the desired product highlight this reaction.



(F) $ZrCl_4$ is an efficient catalyst for the synthesis of α-aminophosphates.[18] The method is effective for aromatic, aliphatic, or α,β-unsaturated aldehydes and provides excellent yields of the product.



(G) The THF complex of $ZrCl_4$ i.e. $ZrCl_4{\cdot}(THF)_2$ is highly effective as a catalyst for the selective esterification of primary alcohols with carboxylic acids in the presence of secondary alcohols or aromatic alcohols.[19] Direct condensation of equimolar amounts of carboxylic acids and alcohols could be achieved using Zr(IV) salts. This method offers considerable advantage in terms of simplicity, high chemoselectivity, high atom efficiency, and low environmental impact.



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