SYNLETT
Spotlight 364

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

1,1,3,3-Tetramethyldisiloxane

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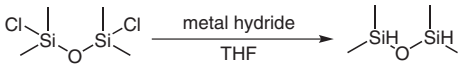
Introduction

1,1,3,3-Tetramethyldisiloxane (TMDS) is a hydrosiloxane derivative and has been used in organic synthesis as a mild reducing agent and intermediate for the preparation of organopolysiloxanes. It is a rather cheap, little hazardous, safe, volatile liquid boiling at 71 °C and is stable towards air and moisture.[1] It has been used as a reducing agent for the direct synthesis of alkyl halides from aldehydes[2] and for the synthesis of alkyl halides from epoxides.[3] It was also found to be a mild donor of hydride for selective semihydrogenation of acetylenes to olefins,[4] it is used for the reduction of aryl chlorides to the corresponding arenes,[5] the reduction of unsymmetrical secondary phosphine oxides to secondary phosphine,[6] the reductive cleavage of inert C–O bonds,[7] and the preparation of aldenamines from carboxamides.[8] The enantioselective reductive Michael cyclization of substrates containing two α,β-unsaturated carbonyl moieties has been achieved by the use of a combination of TMDS and chiral copper–bisphosphine complexes.[9] Reduction and reductive N-alkylation of secondary amides to secondary amines with a ruthenium complex/TMDS system are readily accomplished.[10]

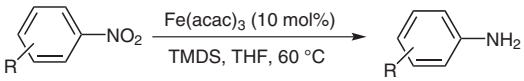
1,1,3,3-Tetramethyldisiloxane is a by-product of the silicon industry and the lowest-molecular-weight commercially available hydrosiloxane derivative now. It can be readily prepared by reduction of 1,1,3,3-tetramethyl-1,3-dichloro-1,3-disiloxane with a metal hydride such as lithium aluminum hydride, sodium aluminum hydride, lithium borohydride, lithium hydride or sodium hydride in tetrahydrofuran.



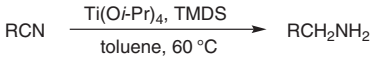
Scheme 1

Abstracts

(A) *Reduction of Nitro Compounds to Amines*:
Pehlivan et al. reported that TMDS can be applied as a mild reducing reagent for direct reductive aromatic nitro compounds to the corresponding amines in the presence of catalytic amounts of $Fe(acac)_3$ in THF at 60 °C. This system has shown a good selectivity toward aryl chloride, aryl bromide, ester, carboxylic acid, and cyano groups. The alkylnitro compounds can not be reduced under the same conditions.[11]



(B) *Reduction of Nitriles to Amines*:
A mild, safe, and efficient reduction procedure for the direct conversion of aromatic and aliphatic nitriles into the corresponding amines using a TMDS/titanium(IV) isopropoxide reducing system in toluene has been developed.[12] The primary amines as hydrochloride salts were obtained in almost quantitative yield.



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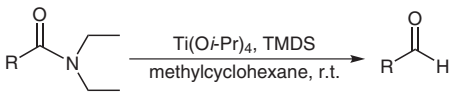
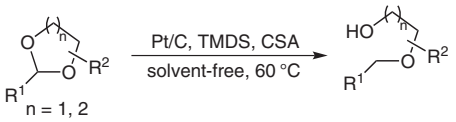
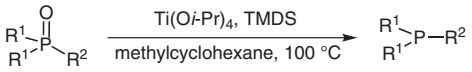
(C) *Reduction of Amides to Aldehydes*:
The above reducing system has also been applied for the reduction of aromatic, as well as aliphatic, tertiary amides to the corresponding aldehydes.[13] The reaction was carried out using 100 mol% of TMDS and 100 mol% of Ti(O*i*-Pr)$_4$ in methylcyclohexane at room temperature.



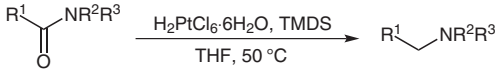
(D) *Reduction of Acetals to Ethers*:
Shi et al. found that TMDS can serve as the hydride source for the reduction of acetals to ethers using Pd/C as the catalyst in the presence of camphorsulfonic acid (CSA) as a promoter.[14]



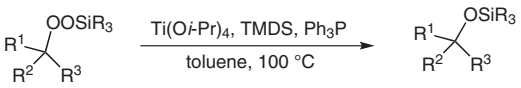
(E) *Reduction of Phosphine Oxides to Phosphines*:
Berthod et al. showed that TMDS is an efficient hydride source for the reduction of tertiary and secondary phosphine oxides to afford the corresponding phosphine in high yields in the presence of catalytic amounts of Ti(O*i*-Pr)$_4$.[15] Electron paramagnetic resonance (ESR) spectra of the reaction mixture gave evidence that this reaction occurred via a single-electron-transfer (SET) mechanism rather than a titanium hydride-like complex.[16]



(F) *Reduction of Tertiary Carboxamides to Tertiary Amines*:
A convenient and practical method for the catalytic reduction of carboxamides to amines by combination of platinum and TMDS in THF has been developed.[17] This system was highly chemoselective, tolerating several functional groups such as NO_2, CN, esters, and halides. This reaction has also been conducted in the presence of [Fe(CO)$_5$] or [Fe$_3$(CO)$_{12}$] under irradiation with a high-pressure mercury lamp.[18]



(G) *Reduction of Silylated Hydroperoxides to the corresponding Silylated Alcohols*:
In addition to the above cases, the combination of Ti(O*i*-Pr)$_4$ and TMDS can be applied as useful terminal reductant for the reduction of protected hydroperoxides to the corresponding silylated alcohols by employing catalytic amounts of phosphine.[19]



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