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Spotlight 107

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

Sodium Borohydride – A Versatile Reducing Agent

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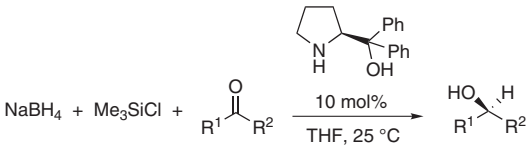
Introduction

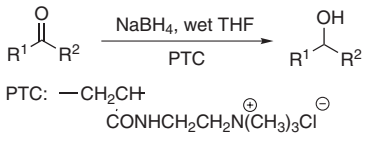
The use of alkali metal borohydrides as reducing agents in organic chemistry is well documented since the pioneering work by H. C. Brown and colleagues.[1] After its first application in carbonyl reduction,[2] sodium borohydride has been widely used as an economical and mild reducing agent in the reduction of carbonyl and related compounds as well as other unsaturated compounds.[3] Suitable substrates[4] included conjugated carbonyl compounds, alkoxysulfonium salts, nitro compounds, carboxylic acids and esters, sulfonate esters, alkyl halides, nitriles, and amides. It was observed that the reducing activity was influenced by solvents and metal ions,[5] and can be finely adjusted by Lewis acid mediation.[6] Reduction in acidic media[7] was investigated extensively. Sodium borohydride ($NaBH_4$) is commercially available as a white crystalline powder with moderate hygroscopic property. It can be used as solution in lower alcohols, or in glymes for elevated temperature. In neutral and acidic water, $NaBH_4$ hydrolyzes to afford hydrogen gas, but a basic aqueous solution of $NaBH_4$ is stable and useful in the lab.

Abstracts

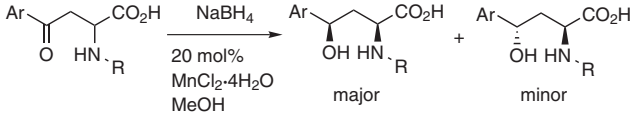
(A) Enantioselective reduction of prochiral ketones by $NaBH_4$ and chiral amino alcohols led to optically active alcohols. The chiral oxazaborolidine-catalyzed reduction (CBS)[8a] of ketones was an important method for secondary chiral alcohol synthesis. Jiang[8b] has shown that (*S*)-α,α-diphenylpyrrolidinemethanol catalyzed the $NaBH_4$ reduction of achiral ketone to afford the chiral alcohol with excellent ee and almost quantitative yield. A similar chiral auxiliary was employed in the reduction of the carbonyl group of α,β-unsaturated ketones.[8c] At the chiral interface of an amphiphilic dendrimer, alcohols were obtained in high ee by reduction of the corresponding prochiral ketones.[8d]



(B) Polymer reagents are useful in $NaBH_4$ reduction. Quaternary ammonium-functionalized cross-linked polyacrylamide was used as a solid–liquid phase transfer catalyst in the reduction of carbonyl compounds with $NaBH_4$.[9a] The resin proved to be efficient in carbonyl reduction and highly regioselective in α,β-unsaturated aldehyde and ketone reduction. A new combination system of Amberlyst-15(H^+)–$NaBH_4$–LiCl[9b] facilitated the reduction of oximes and hydrazones to the corresponding amines and hydrazines.



(C) A highly stereoselective reduction of γ-oxo-α-amino acids by $NaBH_4$ in the presence of a catalytic amount of manganese(II) chloride gives *syn*-γ-hydroxy-α-amino acids.[10] In most reported cases, the dr is higher than 97:3.



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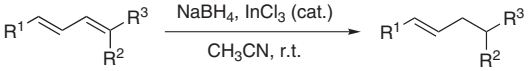
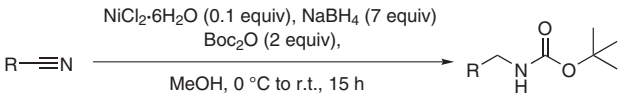
(D) A combination of $NaBH_4$ and a catalytic amount of indium(III) chloride in acetonitrile reduces exclusively the α,β carbon–carbon double bond in α,β,γ,δ-unsaturated diaryl ketones, dicarboxylic esters, cyanoesters, and dicyano compounds.[11a] The same system reduces selectively the carbon–carbon double bonds in activated conjugated alkenes.[11b]

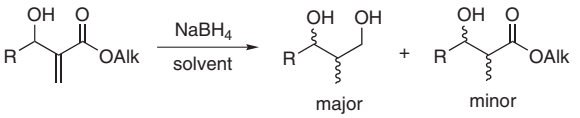


R^1 = Ar; R^2 = H, CO_2Et, CN; R^3 = COAr, CO_2Et, CN

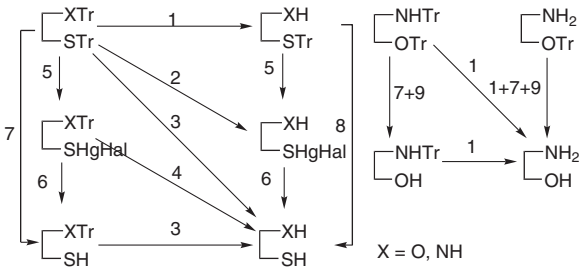
(E) A practical procedure for the catalytic reduction of nitriles to Boc amines[12a] has been developed; it is neither air- nor moisture-sensitive, and is easily worked up. Nitro compounds,[12b] imines,[12c] and azides[12d] are reduced by Lewis acid-assisted $NaBH_4$ to afford amines.



(F) Reduction of the ester group in Baylis–Hillman adducts by $NaBH_4$ is facilitated by the secondary hydroxyl group present at the β-position. This method is efficient for the preparation of substituted propane-1,3-diols.[13]



(G) $NaBH_4$ in combination with Lewis acids is effective in the selective deprotection or cleavage of certain protective groups. A room-temperature deprotection method for trityl amines, trityl ethers, and trityl thioethers was reported.[14a] An efficient and chemoselective deprotection of prenyl ethers of phenols and alcohols with $ZrCl_4/NaBH_4$ in CH_2Cl_2 was achieved in high yields.[14b] *Reagents:* 1. TFA, H_2O; 2. $HgHal_2$/TFA, H_2O; 3. $HgHal_2$/TFA, H_2O, $NaBH_4$; 4. TFA, H_2O, $NaBH_4$; 5. $Hg(OAc)_2$/AcOH, H_2O, $HgCl_2$/MeCN, H_2O; 6. $NaBH_4$/MeCN; 7. $HgHal_2$/MeCN, $NaBH_4$; 8. i. 7 and ii. $NaBH_4$; 9. HCl/MeCN, H_2O.



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