

SYNLETT Spotlight 221

Borane – A Mild, Selective, and Convenient Reducing Agent

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

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Introduction

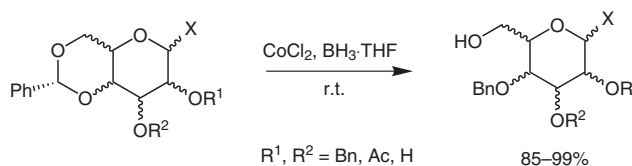
Borane is a powerful, selective, and mild reducing agent with characteristics frequently different from the so-called nucleophilic hydrides. Due to its broad use in organic synthesis for the reduction of amides, nitriles, carboxylic acids and esters, nitroalkenes, ketones, for the hydroboration of alkenes and the reductive cleavage of al-

yl ethers, borane is commercially available in various forms (e.g., $\text{BH}_3\cdot\text{THF}$, $\text{BH}_3\cdot\text{SMe}_2$, and $\text{BH}_3\cdot\text{NR}_3$).

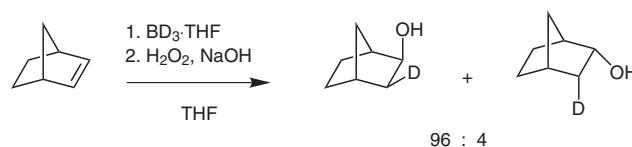
Since its initial use in synthesis by H. C. Brown,¹ several applications of this reactant and its derivatives in diverse chemistry fields have been published.² Actually, advances in borane thermal properties and stability,³ asymmetric reduction using borane in situ,⁴ and kinetic and mechanistic studies⁵ are successfully reported in the literature.

Abstract

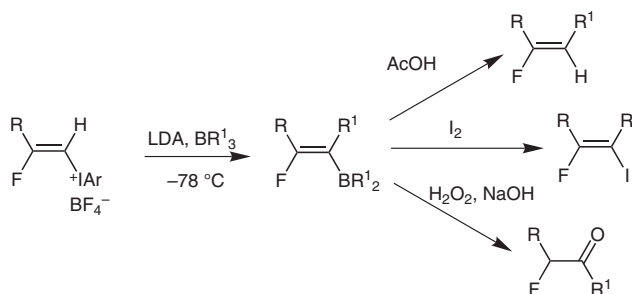
(A) A novel and facile reductive ring-opening reaction for 4,6-*O*-benzylidene acetal derivatives of hexopyranosides using $\text{CoCl}_2/\text{BH}_3\cdot\text{THF}$ gave the corresponding 4-*O*-benzyl-6-OH derivatives selectively in good yields.^{6a} However, regioselective reductions of this compound using $\text{LiAlH}_4/\text{AlCl}_3$,^{6b} DIBAL-H,^{6c} $\text{Me}_2\text{NHBH}_3/\text{BF}_3\cdot\text{Et}_2\text{O}$,^{6d} $\text{V}(\text{O})(\text{OTf})_2/\text{BH}_3\cdot\text{THF}$,^{6e} and $\text{Bu}_2\text{BOTf}/\text{BH}_3\cdot\text{THF}$ ^{6f} are reported. $\text{LiAlH}_4/\text{AlCl}_3$ and DIBAL-H are of limited use due to their effects on acyl groups, which are often used in carbohydrate chemistry.



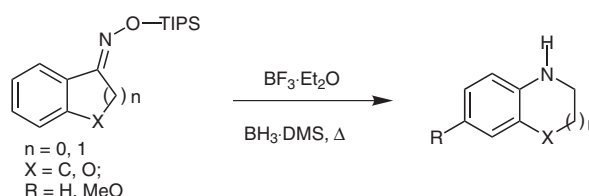
(B) Norbornene and other alkenes suffered hydroboration with $\text{BD}_3\cdot\text{THF}$ at room temperature in THF, then were subsequently oxidized to the corresponding alcohol. $\text{BD}_3\cdot\text{THF}$, stabilized with 0.005 mol% *N*-isopropyl-*N*-methyl-*tert*-butylamine (NIMBA), showed good thermal properties, directly resulting in improved reactant stability for deuterium label incorporations.⁷



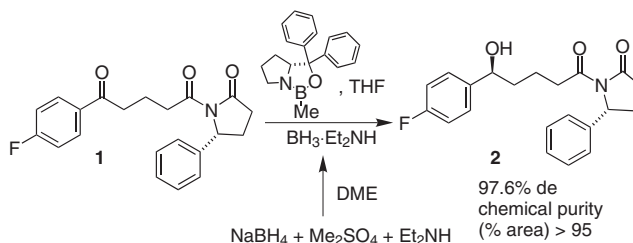
(C) Alkylidene-type carbenoids generated from (*Z*)- or (*E*)-(2-fluoro-1-alkenyl)iodonium salts by treatment with LDA, reacted with trialkylboranes to give (*E*)- or (*Z*)-(fluoroalkenyl)boranes stereoselectively. The resulting (fluoroalkenyl)borane can be used for the selective synthesis of (*Z*)- or (*E*)-fluoroalkenes, (*Z*)- or (*E*)-fluoroiodoalkenes, and α -fluoroketones.⁸



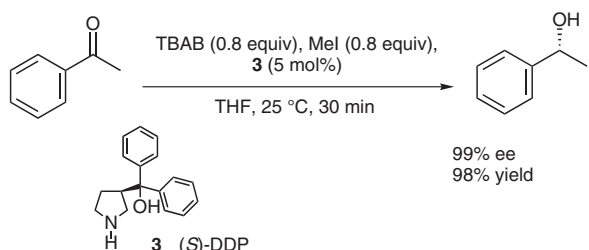
(D) Aromatic *O*-triisopropylsilyl ketoximes were efficiently rearranged to cyclic and acyclic aniline derivatives on reduction with $\text{BF}_3 \cdot \text{Et}_2\text{O}$ /borane. The bulkiness of the groups attached to the silicon atom, the size of the aliphatic ring, and the presence of alkoxy groups on the aromatic ring always play an important role in the amine synthesis.⁹



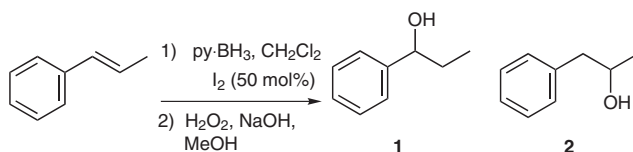
(E) The *S*-alcohol group in the benzylic position of compound **2**, a key intermediate in the synthesis of the cholesterol-lowering agent ezetimibe, was introduced by the (*R*)-MeCBS catalyzed asymmetric carbonyl reduction of ketone **1** using borane diethylaniline complex (BDEA) generated in situ as the reducing agent.¹⁰ BDEA prepared in situ offers considerable advantages from an industrial point of view (cost and stability on storage of the reagents) over commercial solutions of $\text{BH}_3 \cdot \text{THF}$ (BTHF) or $\text{BH}_3 \cdot \text{DMS}$ (BDMS).



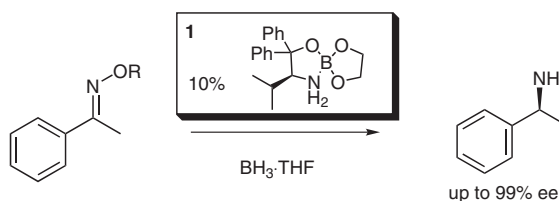
(F) An oxazaborolidine catalyst is readily prepared in situ at 25 °C in THF using (*S*)- α,α -diphenylpyrrolidinemethanol and borane generated from the tetrabutylammonium borohydride/MeI reagent system. The oxazaborolidine/ BH_3 reagent system prepared in this way is useful for the reduction of prochiral ketones to the corresponding alcohols with up to 99% ee.⁴



(G) Diverse hydroborating agents, including $\text{BH}_3 \cdot \text{THF}$, $\text{BH}_3 \cdot \text{Me}_2\text{S}$, 9-BBN, and hexylborane, are readily available and offer many ways for selective hydroboration. However, each one has limitations as well as advantages and all are air-sensitive. The more stable pyridine borane ($\text{py} \cdot \text{BH}_3$) was activated with 50 mol% of I_2 in dichloromethane to generate $\text{py} \cdot \text{BH}_2\text{I}$. Addition of β -methylstyrene followed by oxidative work-up gave alcohol products (92%; **1/2** = 15:1).¹¹



(H) The enantioselective borane reduction of *O*-benzyloxime ethers to primary amines was studied under catalytic conditions using spiroborate esters derived from non-racemic 1,2-aminoalcohols and ethylene glycol. Effective catalytic conditions were achieved using 10% of **1** in dioxane at 0 °C, resulting in complete conversion into the corresponding primary amine in up to 99% ee.¹²



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