ORGANIC SEMINAR

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4:30 PM, WTHR 104

"Lewis Acid Catalyzed Functional Group Transformations Using Borane-ammonia"

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Abstract: While the utilization of borane-ammonia (BA) has played a crucial role in shaping and advancing the field of organic chemistry, we believe the potential applications of BA in organic reductions had not been extensively explored. Our studies aimed to investigate BA as a reducing agent in organic reactions and delve into the associated reduction mechanisms. Initially, we discovered that BA, when used in conjunction with catalytic amounts of titanium tetrachloride ($TiCl_4$, 10 mol%) leads to the hydroboration of various aryl and alkyl ketones, which typically requires 24 h or longer to reduce under uncatalyzed conditions. Moreover, substituted cycloalkanones were reduced diastereoselectively to the thermodynamic product. Another aspect of the study revealed that the catalytic effect of titanium tetrachloride (10 mol %) is successful in catalyzing the direct reduction of a diverse range of aromatic and aliphatic mono- and dicarboxylic acids at room temperature by increasing the stoichiometry of BA. This process, tolerant to various potentially reactive functional groups including N-protected amino acids, allows for the selective reduction of acids in the presence of amides and nitriles.

Additionally, the titanium-system was also applied to deoxygenation of both aromatic and aliphatic carboxylic esters to ethers by regulating the stoichiometry of the reductant, BH_3–NH_3, and the catalyst $TiCl_4$. This first, practical borane-mediated process compatible with a variety of potentially sensitive functional groups and is applicable to deoxygenative ether formation from typically challenging aromatic acid esters. Substituting BF_3–Et_2O as the catalyst alters the reaction pathway, reducing the esters to alcohols.

Furthermore, we have successfully achieved the deoxyhalogenation of aryl aldehydes, ketones, carboxylic acids, and esters using an appropriate metal halide Lewis acid as a carbonyl activator and halogen carrier in combination with borane-ammonia. The selectivity in this process is achieved by matching the stability of the carbocation intermediate with the effective acidity of the Lewis acid. Substituents and substitution patterns were found to significantly influence the requisite solvent/Lewis acid combination. The logical combinations of these factors were also applied for the regioselective conversion of alcohols to alkyl halides.

A systematic examination was also initiated and reported is the facile conversion of both aliphatic and aromatic nitriles to primary amines with borane-ammonia in the presence of a molar equivalent of titanium tetrachloride. This system was extended to the reduction (deoxygenation) of a variety of aromatic and aliphatic pri-, sec- and tert-carboxamides, by changing the stoichiometry of the catalyst and reductant. The corresponding amines were isolated in good to excellent yields, following a simple acid–base workup.

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