ORGANIC SEMINAR

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"Advances in Direct Amidation and Application to Anti-Selective Trifluoromethyl Aldol Synthesis"

Amide bond formation via direct amidation is hindered by ammonium carboxylate salt formation, necessitating activation of the carboxylic acid, amine component, or use of a Lewis acid catalyst. Building on our group's prior contributions, a borane-pyridine catalysed direct amidation protocol was developed at 5 mol% loading, delivering up to quantitative yields. Subsequently, inexpensive ionic inorganic salts were also demonstrated as effective fluoro-inorganic catalysts for direct amidation. However, these protocols suffered from elevated reaction temperatures and prolonged reaction times.

To address these issues, a titanium-mediated room temperature amidation protocol was developed, proceeding near-instantaneously through amido-titanate and titanium carboxylate intermediates to deliver high yields of aliphatic, aromatic, and Weinreb amides under ambient conditions. Finally, leveraging the developed substrate scope, enolboration of α-trifluoromethyl-*N*-methoxy-*N*-methylacetamide was employed to access a series of novel anti-aldol products in high diastereoselectivity from a diverse array of aldehyde and ketones.

PURDUE UNIVERSITY | James Tarpo Jr. and Margaret Tarpo Department of Chemistry

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