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A CHIMIA Column

Short Abstracts of Interesting Recent Publications of Swiss Origin

Synthesis of Secondary and Tertiary Amides without Coupling Agents from Amines and Potassium Acyltrifluoroborates (KATs)

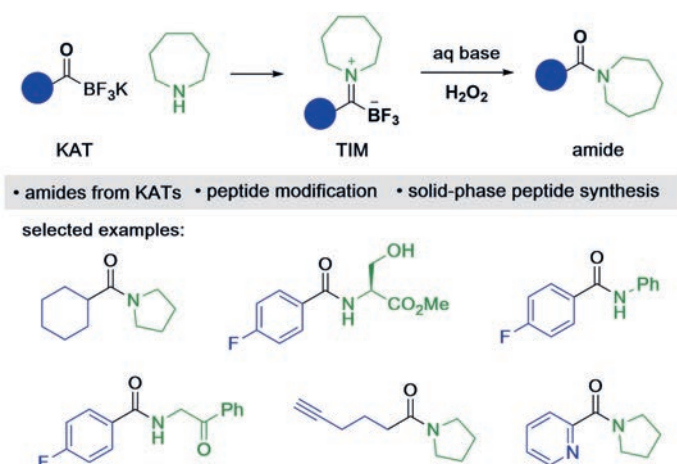
A. Schuhmacher, T. Shiro, S. J. Ryan, and J. W. Bode,* *Chem. Sci.* **2020**, DOI: 10.1039/D0SC01330G.

Eidgenössische Technische Hochschule Zurich

Amide bonds are the key connections between amino acids in peptides and are present in many bioactive substances. However, the synthesis of amides traditionally employs stoichiometric coupling reagents that show significant limitations. The authors report the oxidative synthesis of amides from potassium acyltrifluoroborates (KATs) under aqueous condition *via* the formation of trifluoroborate iminium (TIM) intermediates. TIMs can be isolated from the condensation of KATs and amines or can be generated *in situ* in a one-pot procedure. This method allows for the fast and efficient synthesis of both secondary and tertiary amides and shows a high functional group tolerance. Preliminary studies showed that this method is applicable to the late-stage modification of peptides and to the iterative synthesis of *N*-methylated peptides without coupling agents.

Authors' comments:

"This work is a first step towards an approach to peptide synthesis in which the preformed monomers are assembled without coupling reagents and under conditions where excess amounts of the reaction partners can be readily recovered and reused."



Three-Component Reaction for the Synthesis of Highly Functionalized Propargyl Ethers

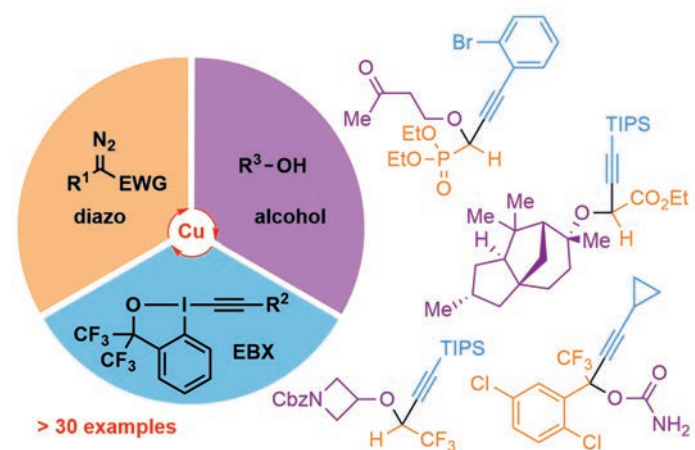
G. Pisella, A. Gagnebin, and J. Waser* *Chem. Eur. J.* **2020**, 10.1002/chem.202001317.

Ecole Polytechnique Fédérale de Lausanne

Multicomponent reactions are important synthetic tools to rapidly build molecular complexity through the use of simple building blocks. Readily available diazo and hypervalent iodine compounds have proven to be versatile components for such reactions, allowing the introduction of a wide variety of substitution patterns. Herein, the Waser group reports a Cu-catalyzed three-component oxyalkynylation protocol, employing hypervalent iodine reagents, alcohols and diazo compounds. A range of highly functionalized and structurally diverse propargyl ethers were obtained under mild conditions. Mechanistic studies support the stepwise formation of a copper carbene and an ylide intermediate, followed by electrophilic alkynylation. This work sets the base for the development of enantioselective variants and the use of other classes of nucleophilic partners.

Authors' comments:

"The high energy of diazo compounds and EBX reagents was harnessed in a copper-catalyzed three-component reaction with alcohols for the construction of structurally diverse propargyl ethers."



Accessing the +IV Oxidation State in Molecular Complexes of Praseodymium

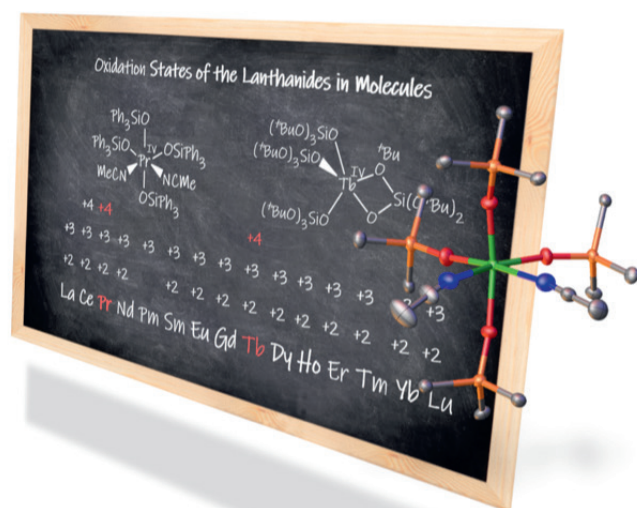
A. R. Willauer, C. T. Palumbo, F. Fadaei-Tirani, I. Zivkovic, I. Douair, L. Maron, and Marinella Mazzanti,* *J. Am. Chem. Soc.* **2020**, *142*, 5538–5542.

Ecole Polytechnique Fédérale de Lausanne, Institut National des Sciences Appliquées

The most stable oxidation state for all lanthanide elements is +III. The authors discovered that the +IV oxidation state is also accessible for the large praseodymium (Pr) cation, in addition to cerium and terbium. In particular, they succeeded to isolate a Pr(IV) complex with electron-rich triphenylsiloxide ligands. To this purpose, they first prepared a Pr(III) ate complex, $[\text{KPr}(\text{OSiPh}_3)_4(\text{THF})_3]$. The addition of the strong oxidizing agent $[\text{N}(\text{C}_6\text{H}_4\text{Br})_3][\text{SbCl}_6]$ to a solution of this ate complex furnished the isolable Pr(IV) complex $[\text{Pr}(\text{OSiPh}_3)_4(\text{MeCN})_2]$. The +IV oxidation state of Pr was unambiguously proven by magnetometry, UV-visible absorption spectroscopy and cyclic voltammetry, and the experimental results were corroborated with DFT calculations. This work extending the +IV oxidation state to praseodymium should open new opportunities in lanthanide chemistry.

Authors' comments:

“The isolation of a molecular Pr(IV) turned out to be much more challenging than for Tb(IV). Overcoming this challenge opens the route to new lanthanide redox chemistry and to the discovery of unexpected physical properties.”



Asymmetric β -Methylation of L- and D- α -Amino Acids by a Self-Contained Enzyme Cascade

C. Liao, and F. P. Seebeck,* *Angew. Chem. Int. Ed.* **2020**, *59*, 7184–7187.

University of Basel

The integration of multiple elementary steps into cascade reaction is a powerful tool for shortening chemical syntheses. Enzymes are particularly well suited for this purpose. However, one of the challenges to overcome is the regeneration of cofactors required for the transformations. The authors report an enzyme-based cascade process that enables the stereoselective synthesis of L- or D- β -methyl- α -amino acids (β -Me- α -aas). A variety of L- β -Me- α -aas were prepared using methyl iodide as the methylation agent in good conversions and high enantioselectivities (up to >95% and 99:1 e.r.). The substrate scope was further expanded by using transaminases and α -keto acid methyltransferases with different substrate specificities. This work is an important step forward in the use of cascade enzymatic process to produce valuable amino acid building blocks.

Authors' comments:

“We believe that β -Me- α -aas are intriguing building blocks for the design of functional peptides and proteins. Hopefully, our methodology will help to make these aas more accessible.”

