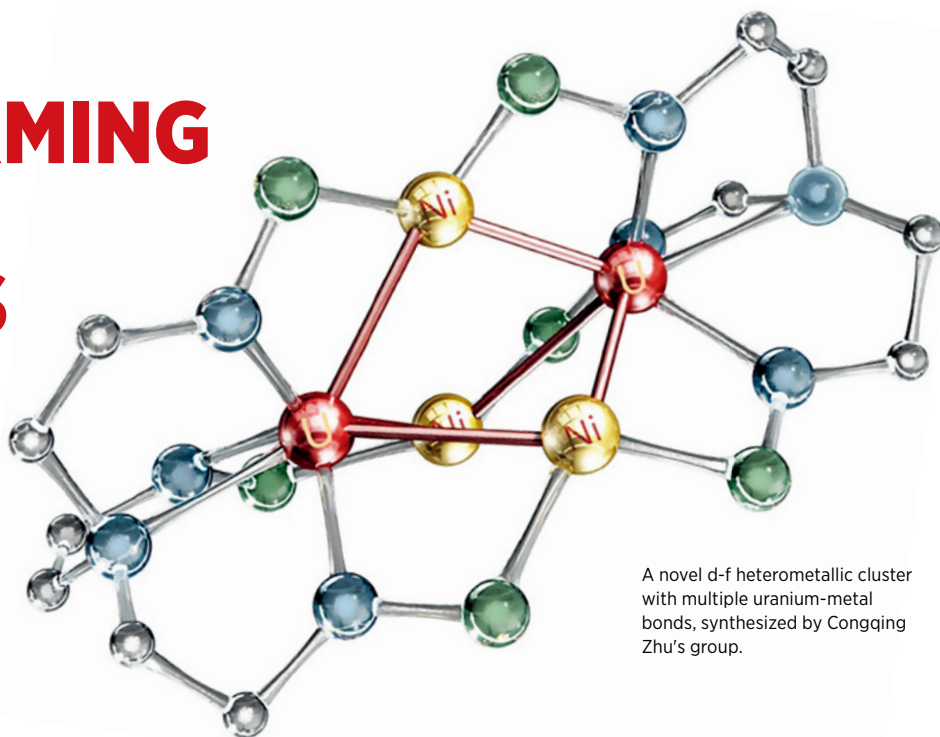


TRANSFORMING CHEMICAL SYNTHESIS

Chemists at Nanjing University are finding new ways to engineer complex molecules.



A novel d-f heterometallic cluster with multiple uranium-metal bonds, synthesized by Congqing Zhu's group.

Advances in synthetic chemistry have made it possible to design and make complex molecular architectures for use in medical, materials, and energy fields. Carbon-hydrogen (C-H) functionalization, a reaction that breaks a C-H bond, is becoming a particularly attractive strategy for transforming organic chemicals, given its many appealing features. Scientists at Nanjing University's School of Chemistry and Chemical Engineering (SCCE) are designing new solutions that push the boundaries of organic synthesis, especially, C-H functionalization.

Site-selective C-H functionalization of alkenes, which are readily available feedstock starting materials, is valuable for synthesis, but challenging. An SCCE team, led by Shaolin Zhu, has developed a solution to achieve this reaction by combining cross-coupling and nickel hydride-catalysed chain-walking, namely, migration of a double bond along the hydrocarbon chain. This is expected to spark the development of other remote functionalizations and asymmetric transformations.

Given the obstacles of cost and possible toxicity of metals, developing metal-free C-H functionalization is attracting interest. Another SCCE team, led by Zhuangzhi Shi, has recently uncovered a strategy for directed C-H borylation of (hetero)arenes under metal-free conditions, using boron tribromide (BBr₃) as the reagent and catalyst. A colourless, fuming liquid compound, BBr₃ is commercially available in quantities from multi-grams to kilograms, and is cheaper than most common boron reagents, making it an attractive choice. This milder and more efficient reaction for transforming formed boron species has potential applications in natural product and drug scaffold synthesis.

Focusing on C-H functionalization reactions under milder conditions, SCCE's Chengjian Zhu and his team have developed C-H functionalization triggered by photocatalysis. With his colleague, Jin Xie, Zhu also designed deoxygenation approaches for synthesizing ketones from aromatic carboxylic acids and alkenes, and for preparing deuterated aldehydes from aromatic and aliphatic carboxylic acids, using deuterium oxide as a source. These strategies are promising for synthesizing drug compounds. Another group, led

by Shouyun Yu, found mild ways to generate nitrogen-centred radicals from hydroxylamine derivatives under photoredox catalysis.

SCCE scientists have also made breakthroughs in total synthesis and organometallics. The team, led by Zhujun Yao, has achieved the first total syntheses of a series of complex bioactive natural products. Their strategies for synthesizing some alkaloids with anticancer functions are efficient and high yielding. These studies shed light on the efficient and economic production of anticancer and influenza drugs. While Congqing Zhu's team established a straightforward strategy to construct a series of heterometallic clusters featuring multiple uranium-metal bonds, showing the first example of an f-block metal-metal triple bond.

Challenging computational limits

Molecular modelling and electronic structure calculations are essential for understanding the behaviour of chemical systems. However, conventional calculation methods often fall short for larger, more complex, systems, as they are too computationally intensive.

For example, traditional quantum chemistry-based methods to calculate ground-state electronic structures are only feasible for medium-sized molecules. To solve this, a team led by SCCE professors, Shuhua Li, Wei Li, and Jing Ma, have proposed energy-based fragmentation and 'cluster-in-molecule' local correlation approaches, enabling *ab initio* investigation of the structures, properties, and reactivity of complex systems with up to thousands of atoms. Haibo Ma and his co-workers also achieved low-cost, excited-state calculations of large molecules, facilitating the study of organic solar cells.

Focusing on quantum reaction dynamics, another team, led by Daiqian Xie, has improved coupled-state approximation to better describe molecular collision dynamics. Their approach significantly reduces computational costs without affecting accuracy.

Using the chain-like structural features of macromolecules, Wenbing Hu's team has developed molecular modelling of polymer crystallization to elucidate the principle of polymer chain-folding. This serves as a prototype model for understanding protein folding, misfolding and unfolding. ■