Achieving Molecular Complexity via Metal-free Domino Reactions

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Keywords: *Domino reaction, one-pot process, organoautocatalysis, quinazolines, o-terphenyls, hexaarylbenzenes*

A domino process is a powerful tool to economically and sustainably build up complex molecular architectures, drastically reducing the number of work-up and purification steps. Recently we developed new metal-free multi-component multi-step domino reactions and one-pot processes for the waste-reducing and cost-effective preparation of versatile frameworks, which otherwise are difficult to access via traditional methods. The developed new methods engage simple and readily available compounds in a wide range of domino reactions to construct, e.g., *azabicycles, quinazolines, quinazoline-thiohydantoins, 2,6-dicyanoanilines, o-terphenyls* and *hexaarylbenzenes* of interest for medicinal chemistry and materials science.[1-4] We recently disclosed a versatile *organoautocatalytic* transamination metathesis reaction, which is a multi-step domino process.[5] This novel methodology gives rapid and atom-economical access to N-substituted 1,4-dihydropyridines, privileged structures in bioactive compounds and pharmaceuticals.

The *in vitro* tests against *multidrug-resistant P. falciparum* strains (Dd2 and K1), human cytomegalovirus (*HCMV*), and *multidrug-resistant* P glycoprotein-overexpressing CEM/ADR5000 leukemia cells revealed the selected domino products and some corresponding artemisinin-containing hybrid compounds as highly active agents, outperforming the clinical reference drugs.[6,7] These results will be discussed in the talk.

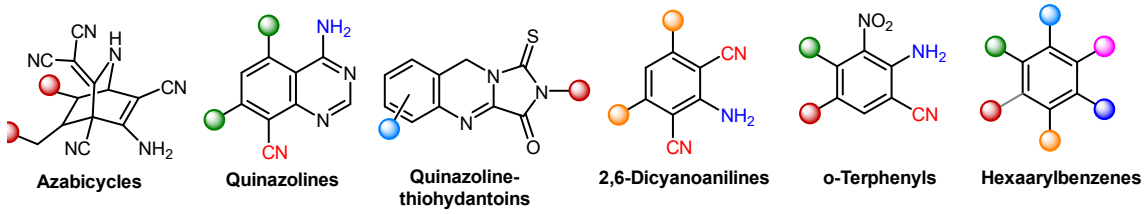

Fig. 1 Compounds prepared via new metal-free multi-component multi-step domino reactions.

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