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ГЕТЕРОЦИКЛЫ В ФОКУСЕ

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Recent advances in the synthesis and synthetic applications of 1,2,3-triazoles (microreview)

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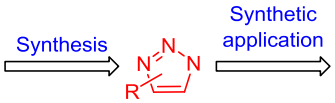


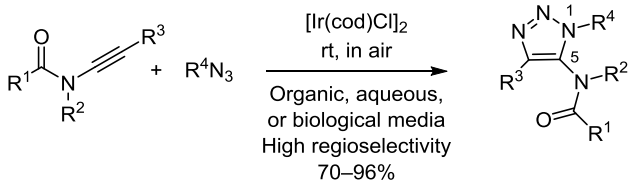
This microreview details recent advances in the synthesis and synthetic applications of 1,2,3-triazole derivatives, which have been published over the last two years.

Introduction

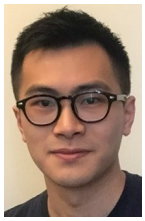
1,2,3-Triazole is an important structural motif in several biologically active compounds and pharmaceuticals (for example, the protein kinase inhibitor mubritinib and antibiotic tazobactam). It also finds applications in dyes, optical brightening agents, and photostabilizers of polymers. The 1,2,3-triazole ring can be present as a monocyclic moiety or fused to some other carbocycles or heterocycles, such as in the case of benzotriazoles. The most common approach for the construction of 1,2,3-triazoles relies on Huisgen 1,3-dipolar cycloaddition between azides and internal alkynes. Several interesting synthetic strategies have been recently developed for the synthesis of highly substituted and fused 1,2,3-triazole derivatives.

5-Amido fully substituted 1,2,3-triazoles

A highly regioselective method for the synthesis of 5-amido fully substituted 1,2,3-triazoles *via* iridium-catalyzed azide-ynamide cycloaddition has been developed by Song et al.[1] The regioselectivity of this reaction is believed to originate from the strong coordination between the carbonyl oxygen of ynamide and the π-acidic iridium catalyst. Furthermore, this reaction is compatible with air, moisture, and the conditions encountered in biorthogonal applications.



R^2, R^3, R^4 = alkyl, aryl; R^4 = carbohydrate

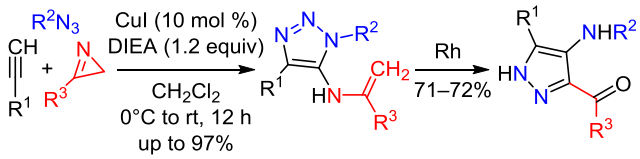


Shengjia Lin was born in 1993 in Guangdong, China. He obtained his BSc (2016) in applied chemistry from the South China Agricultural University. Currently he is doing graduate research in Prof. Abhishek Sharma's laboratory in the Department of Chemistry and Chemical Biology at the Stevens Institute of Technology, Hoboken, NJ, USA. His research is focused on the development of novel synthetic methodologies for biologically important compounds and the discovery of novel anticancer agents.

Abhishek Sharma completed his Ph.D. in organic chemistry at CSIR-IHBT, India. He was a postdoctoral fellow at the University of Leuven (KU Leuven), Belgium, working in the area of transition metal-catalyzed heterocyclic chemistry. Thereafter, he moved to the University of Illinois at Urbana-Champaign, where his postdoctoral research focused on the development of chemical tools for probing the biosynthesis and pharmacology of antibacterial natural products and medicinal chemistry of estrogen receptor antagonists. Currently, he is an Assistant Professor in the Department of Chemistry and Chemical Biology at the Stevens Institute of Technology, Hoboken, NJ, USA. The overarching goal of his lab is to design and develop novel molecular reactivity and molecular function to ultimately accelerate the discovery of new therapeutics.

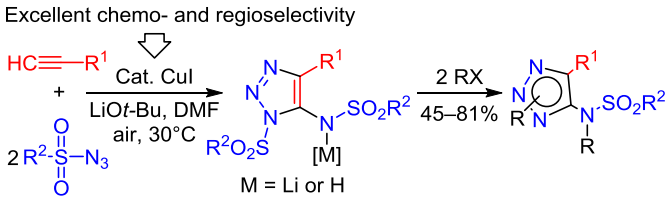
Enamine-functionalized 1,2,3-triazoles

Synthesis of enamine-bearing polysubstituted 1,2,3-triazoles from terminal alkynes, azides, and 2*H*-azirines was achieved in excellent yield by Chen and coworkers, using a Cu-catalyzed interrupted click reaction, in which the triazolyl-Cu intermediate was captured by the 2*H*-azirine rather than a proton.[2] Furthermore, the resulting aminotriazoles could be converted to pyrazoles in the presence of rhodium.



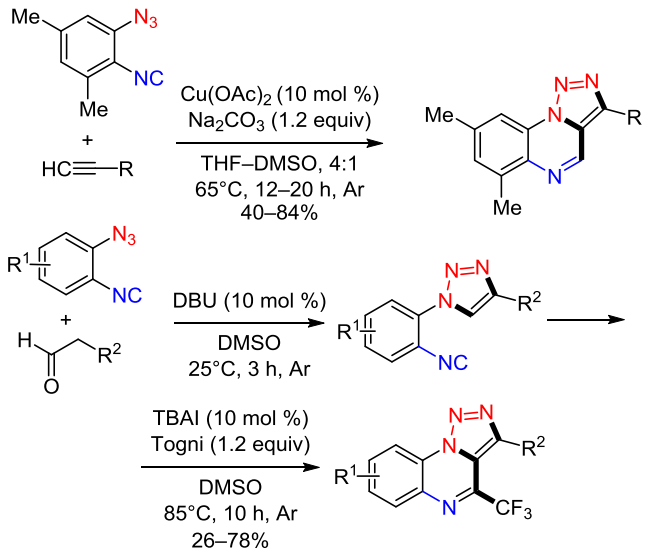
Assembly of substituted aminotriazoles

Ma and coworkers described a regioselective Cu-catalyzed tandem reaction between two equivalents of sulfonyl azide and one equivalent of terminal alkyne that was followed by an alkylation/desulfonation sequence to provide expedient access to a variety of highly substituted aminotriazoles.[3] The authors hypothesized that the reaction mechanism involved high-valent Cu(III) species or copper-nitrenoid intermediates.



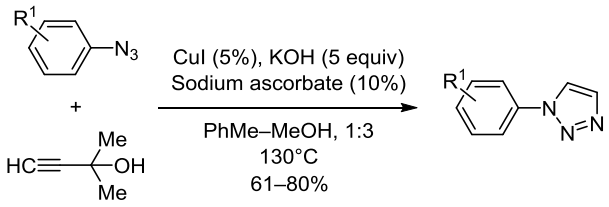
[1,2,3]Triazolo[1,5-*a*]quinoxalines

The [1,2,3]triazolo[1,5-*a*]quinoxaline scaffold is a component of certain benzodiazepine and adenosine receptor inhibitors. The classical method for the synthesis of [1,2,3]-triazolo[1,5-*a*]quinoxalines requires multiple steps. Li et al. described a novel one-pot reaction that provided variously substituted [1,2,3]triazolo[1,5-*a*]quinoxalines from 1-azido-2-isocyanoarenes and terminal alkynes or substituted acetaldehydes under mild conditions.[4] Furthermore, densely functionalized quinoxalines were also obtained from triazole-containing molecules through rhodium-catalyzed N–H or O–H insertion into the carbenoid intermediates.



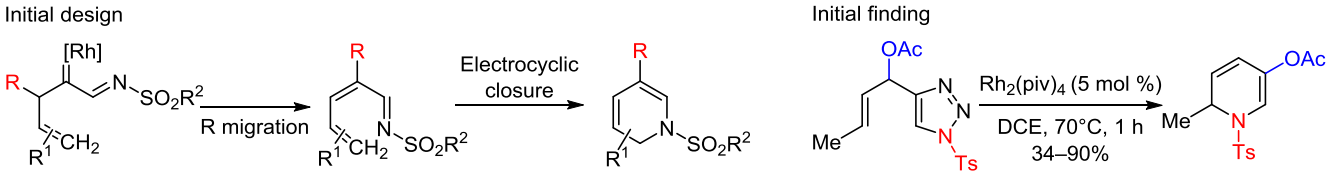
1-Monosubstituted 1,2,3-triazoles

The majority of currently known synthetic approaches for the preparation of 1,2,3-triazoles are focused on disubstituted products. However, the construction of monosubstituted 1,2,3-triazoles is more challenging due to the requirement for acetylene starting material in combination with forcing reaction conditions. Liu et al. reported a new one-step one-pot synthetic method for the preparation of 1-monosubstituted 1,2,3-triazoles using aryl azides and 2-methylbut-3-yn-2-ol as the starting materials in the presence of a copper catalyst, KOH, and sodium ascorbate.[5]



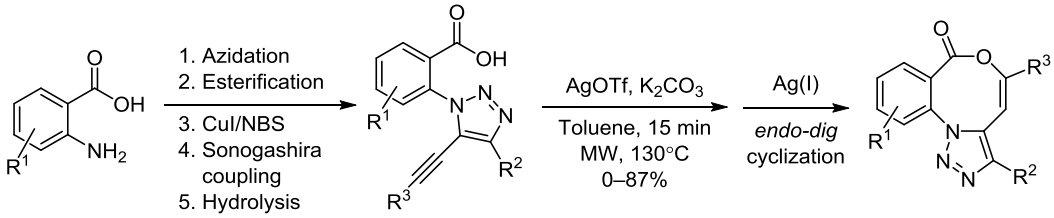
Rhodium-catalyzed tandem reactions of 4-(1-acetoxyallyl)-1-sulfonyl-1,2,3-triazole

Ring-chain tautomerism between the readily available 1-sulfonyl-1,2,3-triazole and α-diazo imine can be used to obtain α-imino rhodium carbenes. The 1,3-dipole nature of these α-imino rhodium carbenes enables their use in annulation reactions with various substrates. However, a major side reaction during these transformations is 1,2-hydride migration. In order to overcome this drawback, Dai et al. installed a good leaving group (OAc) on the α-imino rhodium carbene and used it for the synthesis of *meta*-substituted dihydropyridines *via* a rhodium-catalyzed tandem reaction of 4-(1-acetoxyallyl)-1-sulfonyl-1,2,3-triazole.[6]



Triazole-fused 1,5-benzoxazocinones

Triazole-fused polycyclic heterocycles are found as important structural motifs in various biologically active compounds. There are several strategies for the synthesis of 1,2,3-triazoles annulated at positions 1 and 5 with other heterocyclic systems. Synthetic access to 1,2,3-triazole-fused benzoxazocinones has received less attention. Barve et al. developed regioselective synthesis of novel 1,2,3-triazole-fused benzoxazocinones *via* intramolecular cyclization of substituted ethynyl triazoyl benzoic acids.[7] This intramolecular 8-*endo-dig* cyclization was catalyzed by AgOTf and afforded 7*H*-[1,2,3]triazolo[1,5-*a*][5,1]benzoxazocin-7-ones.



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