Editorial for the Special Topic on C–H Bond Functionalization of Heterocycles

Tharmalingam Punniyamurthy*[a]
Anil Kumar*[b]

[a] Indian Institute of Technology Guwahati, Guwahati-781039, Assam, India
tpunni@iitg.ac.in
[b] Department of Chemistry, Birla Institute of Technology and Science Pilani, Pilani Campus, Rajasthan 333031, India
anilkumar@pilani.bits-pilani.ac.in

DOI: 10.1055/s-0040-1720084; Art ID: SS-2023-0820ED
Published online: 17.10.2023

Received: 14.08.2023
Accepted after revision: 14.08.2023

Tharmalingam Punniyamurthy, Anil Kumar

Over the past few years, direct C–H functionalization has become an extremely powerful synthetic tool for organic synthesis and continues to attract significant attention from organic chemists as it removes the need for pre-functionalization steps, thereby promoting step- and atom-economy.

Moreover, heterocycles constitute a wide family of organic compounds, having impact in all areas of organic, bio-organic and medicinal chemistry. The recent surge in research interest on heterocycles can be attributed to their structural complexity and functional utility, with novel methods for their syntheses and functionalization having been developed. In this realm, innovative methodologies for C–H functionalization have greatly influenced heterocycle synthesis. These new methodologies allow further exploration of the chemical space of heterocycles, thus enabling investigations of their bioactivities and material properties.

This special topic on 'C–H Bond Functionalization of Heterocycles' features original and review articles that highlight important synthetic advancements in direct C–H functionalizations that lead to diversification of heterocyclic compounds. Improved catalytic systems and site-selective C–H functionalization of heterocycles form an important part of this special topic. A total of 5 reviews and 19 articles are included in this issue, highlighting the functionalization of a broad range of heterocycles.

Taskesenligil and Saracoglu have reviewed recent advances on the site-selective C6-H bond functionalization of indoles by remote C–H activation and hydrogen bond formation, while Chattopadhyay and co-workers have reviewed recent developments on the C–H bond silylation of heteroarenes, with an emphasis on the diverse catalytic systems developed and mechanistic studies. Punniyamurthy's group has reviewed the recent advances on the C8-functionalization of quinolines and 1,2,3,4-tetrahydroquinolines via transition-metal-catalyzed chelation-assisted C–H activation. Meanwhile, Gramage-Doria and Bruneau have reviewed the transition-metal-catalyzed C–H activation approach for the construction of carbon–carbon bonds by utilizing diazine and benzodiazine cores. Furthermore, Barker, Wanic and Melvin have reviewed zinc-mediated C–H metalations in organic synthesis.

Liu and Doucet have presented a Pd-catalyzed heteroarylation of 1,2-dihalobenzenes, converging the scope and limitations of the developed strategy. Regioselective C-arylations and C,N-diarylations of phthalazines have been performed by Sakhuja's group under ligand-driven Pd-catalysis to give bi(hetero)aryl products. Furthermore, Nguyen groups has demonstrated a Pd-catalyzed, C7-selective heteroarylation of pyrazolopyrazines to generate bi(hetero)aryl motifs by utilizing a broad range of heteroaryls and aryl iodides.

Babu and co-workers have accomplished a Pd-catalyzed site-selective C–H functionalization of carbazoles using a bidentate directing group, whilst the Altman group has showcased a Pd-catalyzed C2–H functionalization of benzothiophenes enabled by an uncommon dearomatization–rearomatization pathway. Krishna Singh's group has developed a Pd-catalyzed decarboxylative alkenylation of imidazopyridines with α,β-unsaturated carboxylic acids.

Satoh and co-workers have presented an efficient method for the direct synthesis of thienopyrroles via a Rh-catalyzed direct annulation, while the team of Roger and Hierso has described a phosphorous-directed, Rh-catalyzed *peri* C–H

© 2023. Thieme. All rights reserved.

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.

arylation of polyaromatic compounds. In addition, Ramana's group has presented a Rh-catalyzed alkenylation/alkylation of the pyrazolyl core of GBT-440 by employing a pyridyl directing group. Ramkumar and Gandhi have reported an expedient Ru-catalyzed C–H hydroxyalkylation to achieve biologically pertinent functionalized phthalazinones via a greener pathway. In addition, Wan and Sun have described an efficient Rh-catalyzed C–H homoallylation of indolines to give homoallylic alcohols with excellent stereoselectivities.

The group of Silva and Marques has reported a Mn/Ni-Pd bimetallic system for the synthesis of 2-arylindoles by integrating oxidation, condensation, and annulation reactions and utilizing alcohols and anilines as the substrates, while Kumar's group has showcased a Mn-catalyzed C–H hydroalkylation of heteroaromatic compounds under mild and additive-free conditions. Furthermore, Kerr's group has achieved an Ir-catalyzed C8-labelling of quinoline *N*-oxides with a low catalyst loading to give deuterated scaffolds. An efficient Au-catalyzed annulation of alkynyl norbornenes has been developed by Joo et al. to furnish benzofused (hetero)arenes, highlighting the importance of steric and electronic factors.

Sartillo-Piscil's group has discussed nonmetallic, TEMPO-mediated selective C(sp^3)–H functionalization of *N*-benzylpiperidines as sustainable alternatives, whilst Fruit and co-workers have developed a sustainable, visible-light-mediated, photocatalyst-free C–H perfluoroalkylation as a straightforward approach to functionalized quinozalinones. Ravi Singh and co-workers have described a sustainable visible-light-mediated C2–H selenation of 3-substituted indoles. In addition, Bagdi's group has described a photocatalyst-free, visible-light-mediated regioselective C–H selenylation of pyrazolo[1,5-*a*]pyrimidines.

As mentioned above, the collection of excellent reviews and articles featured in this special topic, from leaders and experts in the community, highlights the advances in the field of direct C–H bond functionalization of heterocyclesn under transition-metal-catalysis and metal-free conditions. The publisher and we would like to thank all the contributing authors for accepting our invitation and all the reviewers for participating in the peer-review process.

We sincerely hope that the articles published within this special topic on the 'C–H Bond Functionalization of Heterocycles' will be of considerable interest to researchers in the field of organic synthesis and medicinal chemistry. The outlook for future research on this topic is promising, and it is foreseeable that the application of photoredox, electrochemical and mechanochemical conditions will offer excellent opportunities to develop additional site-selective C–H functionalizations of heterocycles under milder conditions.

Tharmalingham Punniyamurthy
Anil Kumar
August 2023

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.