
List of Publications

I. Journals:

Included in the thesis

- [1] **Bhattacharjee, P.** and Bora, U. Molecular iodine-catalyzed selective C-3 benzylation of indoles with benzylic alcohols: a greener approach toward benzylated indoles. *ACS Omega*, 4(7):11770-11776, 2019.
- [2] **Bhattacharjee, P.**, Boruah, P. K., Das, M. R., and Bora, U. Direct C–H bond activation: palladium-on-carbon as a reusable heterogeneous catalyst for C-2 arylation of indoles with arylboronic acids. *New Journal of Chemistry*, 44(19):7675-7682, 2020.
- [3] **Bhattacharjee, P.**, Dewan, A., Boruah, P. K., Das, M. R., Mahanta, S. P., Thakur, A. J., and Bora, U. Bimetallic Pd–Ag nanoclusters decorated micro-cellulose bio-template towards efficient catalytic Suzuki–Miyaura coupling reaction of nitrogen-rich heterocycles. *Green Chemistry*, 24(18):7208-7219, 2022.
- [4] **Bhattacharjee, P.**, Dewan, A., Boruah, P. K., Das, M. R., and Bora, U. Pd(0)-embedded-lignocellulosic nanomaterials: a bio-tailored reusable catalyst for selective C2–H arylation of free N–H indoles. *Sustainable Chemistry and Pharmacy*, 33:101087, 2023.
- [5] **Bhattacharjee, P.**, Sarma, B., and Bora, U. Molecular-iodine catalyzed selective construction of cyclopenta[*b*]indoles from indoles and acetone: a green gateway to indole-fused cycles. *Organic & Biomolecular Chemistry*, 21(46):9275-9285, 2023.

Not included in the thesis

- [1] Das, S. K., **Bhattacharjee, P.**, and Bora, U. Ascorbic acid as a highly efficient organocatalyst for *ipso*-hydroxylation of arylboronic acid. *ChemistrySelect*, 3(7):2131-2134, 2018.
- [2] Laskar, K., **Bhattacharjee, P.**, Gohain, M., Deka, D., and Bora, U. Application of bio-based green heterogeneous catalyst for the synthesis of arylidinemalononitriles. *Sustainable Chemistry and Pharmacy*, 14:100181, 2019.

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- [3] Dewan, A., Sarmah, M., **Bhattacharjee, P.**, Bharali, P., Thakur, A. J., and Bora, U. Sustainable nano fibrillated cellulose supported in situ biogenic Pd nanoparticles as heterogeneous catalyst for C–C cross coupling reactions. *Sustainable Chemistry and Pharmacy*, 23:100502, 2021.
- [4] Das, S. K., **Bhattacharjee, P.**, Sarmah, M., Kakati, M., and Bora, U. A sustainable approach for hydration of nitriles to amides utilising WEB as reaction medium. *Current Research in Green and Sustainable Chemistry*, 4:100071, 2021.

Review Articles

- [1] **Bhattacharjee, P.** and Bora, U. Organocatalytic dimensions to the C–H functionalization of the carbocyclic core in indoles: a review update. *Organic Chemistry Frontiers*, 8(10):2343-2365, 2021.
- [2] Das, M. R., Hussain, N., Duarah, R., Sharma, N., Sarmah, P., Thakur, A., **Bhattacharjee, P.**, Bora, U., and Boukherroub, R. Metal nanoparticles decorated two-dimensional nanosheets as heterogeneous catalysts for coupling reactions. *Catalysis Reviews*, 2022. DOI: 10.1080/01614940.2022.2100633

II. Book Chapters:

- [1] **Bhattacharjee, P.** and Bora, U. Nanocatalytic carbon-carbon coupling reactions. In *Advanced Nanocatalysis for Organic Synthesis and Electroanalysis*, pages 24-43, ISBN 978-981-5040-16-6. Bentham Science Publishers Ptd. Ltd., 2022.
- [2] Konwar, D., **Bhattacharjee, P.**, and Bora, U. Graphene as a support in heterogeneous catalysis. In *Graphene-Based Nanomaterial Catalysis*, pages 58-77, ISBN 978-981-5040-49-4. Bentham Science Publishers Ptd. Ltd., 2022.

List of Conferences (as Abstract)***Oral Presentation***

- [1] **Bhattacharjee, P.**, Das, S. K., and Bora, U. Ascorbic acid as an efficient organocatalyst for the *ipso*-hydroxylation of arylboronic acids to phenols. National Seminar on Recent Trends in Environmental Responsive Chemical Processes (RTERCP-2017), organized by Department of Chemistry, Debraj Roy College, Golaghat, 22nd-23rd September, 2017.


Poster Presentation

- [1] **Bhattacharjee, P.**, Laskar, K., Gohain, M., Deka, D., and Bora, U. Towards Knoevenagel condensation using bio-based sustainable heterogenous catalyst. OrganiX-2018: An International Conference in Chemistry, organized by Department of Chemical Sciences, Tezpur University, 20th-21st December, 2018.
- [2] **Bhattacharjee, P.** and Bora, U. Palladium-on-carbon as a reusable heterogeneous catalyst for C2-arylation of indoles with arylboronic acids *via* C-H bond activation. International Conference on Emerging Trends in Chemical Sciences (ETCS 2020), organized by Department of Chemistry, Gauhati University, Guwahati, 13th-15th February, 2020.
- [3] **Bhattacharjee, P.** and Bora, U. A Green metal-free approach towards selective C3-Benzylation of Indoles using molecular iodine as a catalyst. First virtual J-NOST symposium; XVI-J-NOST, organized by Indian Institute of Science, Bangalore, 31st October-1st November, 2020.
- [4] **Bhattacharjee, P.** and Bora, U. Palladium-on-carbon catalyzed regioselective C-H functionalization of indoles with arylboronic acids. International Conferences on The Present and Future of Excellence in Organic Synthesis (PFEOS-2021) (virtual mode), organized by Department of Chemical Sciences, Tezpur University, Assam, 7th-8th January, 2021.

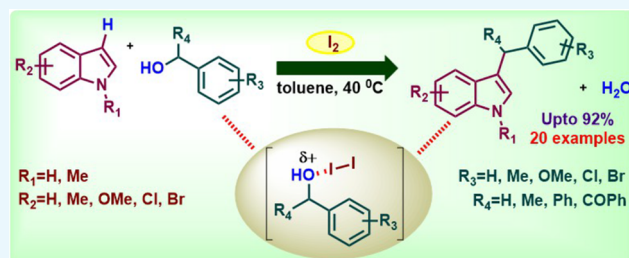
Molecular Iodine-Catalyzed Selective C-3 Benzylolation of Indoles with Benzylic Alcohols: A Greener Approach toward Benzylated Indoles

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 Supporting Information

ABSTRACT: Iodine-catalyzed selective C-3 benzylolation of indoles with benzylic alcohols is developed. The reaction proceeds with molecular iodine as the catalyst under ligand-, metal-, and base-free conditions and tolerates wide functionalities. The experimental observations account for the halogen-bond activation mechanistic pathway for the molecular iodine catalysis.



INTRODUCTION

Heterocyclic compounds are the core building units for the design and synthesis of new molecular entities for drug discovery. Among the myriad of bioactive molecules, a large number of molecules encompass indole derivatives.¹ Substituted indoles are of immense interest as they found applications as pharmaceuticals, drugs, agrochemicals, and in materials science.² Most of the biologically relevant indole alkaloids are C-3-substituted, for example, natural amino acid tryptophan and the neurotransmitter serotonin.³

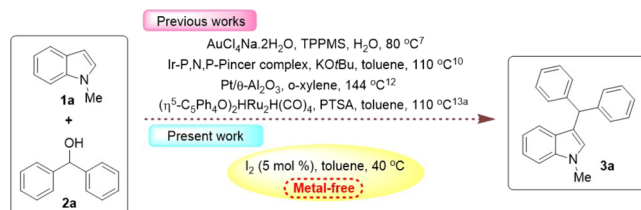
Traditionally, C-3 benzylolation of indoles was achieved mainly via Friedel–Crafts reactions or S_N2 reaction of benzyl halides with indoles.⁴ However, the use of a stoichiometric amount of Lewis acids and formation of unwanted by-products reduce the effectiveness of these methodologies.⁵ Therefore, the demand for mild, efficient, and economic methods for the direct alkylation of indoles remains an area of active research.⁶

Benzylic alcohols are gaining interest as green alkylating agents as the only by-product generated is water, thereby producing an environmentally benign and clean process⁷ compared to the use of corresponding halides, esters, carboxylates, or related compounds for this purpose.⁸

In the past few years, many studies have reported the C-3 benzylolation reactions by using expensive transition metal complex based catalytic systems with Fe,⁹ Ir,¹⁰ Au,⁷ In,⁸ Pd,¹¹ Pt,¹² and Ru,¹³ which are moisture- and air-sensitive,^{8,9} and their preparation process needed complex handling^{10,12} and harsh conditions,^{8,10,12} which limit their practical utility in a large scale. Some methods required the addition of oxidants, ligands,^{7,10} bases,^{9,10} or other additives¹³ to maximize the catalyst activity and complete their catalytic pathway. Metal-free processes are always favorable in the pharmaceutical industry due to the additional difficulties associated with the metal impurities.¹⁴

Therefore, there is rising demand for the development of metal-free catalytic systems for C-3 benzylolation, which has been less explored to date and will be a beneficial alternative to transition-metal catalysis. Yus and co-workers have reported noncatalytic C-3 alkylation by alcohols through a hydrogen-autotransfer strategy with a stoichiometric amount of base.¹⁵ There are reports of C-3 benzylolation catalyzed by Br_2 ,¹⁶ N-heterocyclic carbene,¹⁷ high-temperature water,¹⁸ and some Lewis¹⁹ and Brønsted acids.²⁰ In recent times, molecular iodine has emerged as a green and environmentally benign reagent and has been successfully employed as a catalyst in different organic transformations forming new C–C, C–N, C–O, and C–S bonds in organic compounds.²¹ It is naturally abundant, inexpensive, nontoxic, environmentally friendly, and active even in very small amounts.²² Inspired by its catalytic activeness and economic viability,²³ we herein report a green, efficient, and economical strategy for C-3 selective benzylolation of indoles employing molecular iodine as a catalyst under ligand-, metal-, and base-free conditions (Scheme 1).

Scheme 1. C-3 Benzylolation of 1-Methylindole (1a)



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Direct C–H bond activation: palladium-on-carbon as a reusable heterogeneous catalyst for C-2 arylation of indoles with arylboronic acids†

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Direct C(sp²)-H bond functionalization of indoles with arylboronic acids is achieved using palladium supported on carbon as a reusable heterogeneous catalyst in the presence of an oxidant under mild conditions. The current protocol formed exclusive C-2 selective products without the aid of any ligand or directing group. The catalyst is reusable for up to four catalytic cycles with the retention of catalytic efficiency.

Introduction

Arylated indole moieties are a fascinating class of heterocyclic compounds with pronounced interest for their wide array of biological and pharmaceutical activities, including their anti-bacterial, cytotoxic, anti-oxidative, anti-cancer, and anti-inflammatory properties.¹ Over the last several decades, immense efforts have been devoted to the construction of arylated indoles based on traditional cross-coupling reactions which often requires a multi-step synthetic procedure.² Hence, transition metal catalyzed C–H activation has emerged as an influential means for the direct functionalization of unactivated C–H bonds forming a new C(sp²)-C(sp²) bond in an atom- and step-economic way and has found applications in modern drug research. It empowers previously impossible transformations, new selectivity and shortened reaction paths.³

In this framework, various coupling species have been used in the arena of C–H arylation of indoles and pyrroles using aryl halides,⁴ hypervalent iodine electrophiles⁵ and arylsiloxanes.⁶ Despite significant advantages, there occurs certain limitations such as high reaction temperature, acidic medium, long reaction times, use of ligands and directing groups.⁷ Compared to other coupling partners, organoboronates have some unique advantages including their non-toxicity, high stability, environment-friendly nature and ease of availability.⁸ Therefore, the development of mild and efficient methods for regioselective direct C–H arylation of indoles requires extensive research.

In recent times, many literature studies have reported the metal-mediated selective C-2 arylation of indoles with organo-borane reagents. Various transition metal complex based catalytic systems with Pd,⁹ Rh,¹⁰ Ru,¹¹ Cu,¹² and Co¹³ have been used in this regard. Shi and co-workers have reported the direct construction of C–C bonds through Pd(OAc)₂-catalyzed cross coupling of electron-rich indoles with aryl boronic acids in acetic acid under 1 atm of O₂.¹⁴ Hong and co-workers have presented Pd(OAc)₂-catalyzed direct arylation of electron-deficient polyfluoroarenes with arylboronic acids in DMA at 110 °C.¹⁵ However, most of these reported methods require the use of acidic solvents,¹⁴ high reaction temperatures¹⁵ and an expensive metal catalyst in homogeneous forms which causes difficulties in separation and recovery, which pollutes the environment with heavy metallic ions and is not cost effective. In contrast, heterogeneous catalysts provide ease of separation and the possibility of catalyst recyclability. To date, only a few literature studies have been available for direct C–H arylation of indoles using heterogeneous Pd catalysts.¹⁶ Palladium-on-carbon can offer a beneficial alternative to conventional homogeneous catalysis for C–H arylation of indoles. Compared to other expensive and air-sensitive Pd catalysts, Pd/C exhibits suitable properties such as ease of handling, availability, easy recovery and reusability.¹⁷ It has been successfully utilized as a catalyst in various coupling reactions including Suzuki–Miyaura coupling¹⁸ and decarbonylation, hydrogenation and hydrogenolysis.¹⁹ Inspired by these reports, we hoped to determine its catalytic activeness in C-2 arylation of indoles with arylboronic acids in the absence of any ligands or directing groups (Scheme 1).

Results and discussion

C–H arylation of *N*-methylindole with phenylboronic acid was chosen as the model reaction and the optimization is outlined in Table 1. In the presence of 10% Pd/C (0.05 mmol, 5.3 mg)

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Bimetallic Pd–Ag nanoclusters decorated micro-cellulose bio-template towards efficient catalytic Suzuki–Miyaura coupling reaction of nitrogen-rich heterocycles†

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Cellulose fibers (width 8 μm) were extracted from the waste feedstock of pomegranate peels in a simple filtration method using a water–ethanol system, without any harsh chemical pre-/post-treatments or techniques. The micro-fibrous network of cellulose functions as a true bio-template for Pd–Ag bimetallic nanoclusters and its formation is substantiated by standard analytical studies. The interfacial electron-transfer from the plasmonic metal Ag to Pd makes the newly developed heterogeneous-catalyst suitable for room temperature Suzuki–Miyaura coupling of nitrogen-rich heterocycles (74–93%) under visible light conditions. The enhanced catalytic activity, stability, and recyclability for at least six cycles resulted from the synergistic interactions between bimetal-centres *via* a localized surface plasmon resonance effect. The low energy input throughout the process holds potential for a sustainable transition from laboratory to large-scale nano-material production.

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Introduction

Owing to the importance and widespread applicability of Suzuki–Miyaura cross coupling reactions, the development of efficient catalytic strategies and extension of substrate scope for the reaction, in line with green chemistry principles, is of immense significance and interest.^{1–3} Subsequently, the development of ligand-free heterogeneous catalysts using bio-based renewable supports has become important.⁴ Among the various bio-based supports used, cellulose is unique in terms of its high abundance, chemical inertness, high specific surface area, dimensional stability, available surface functional bonds, and biodegradability.^{5,6} In recent times, successful extraction of cellulose in micro- and nano-crystalline forms⁷ has rendered its use as a support template for various metallic nanoparticles (NPs) such as Pd,^{8,9} Au,¹⁰ Ag,¹¹ and bi-metallic Fe–Cu,¹² Ag–Cu,¹³ and Ag–Au,¹⁴ NPs. Thus, cellulose in the

form of nanostructures has been celebrated as one of the most prominent green templates for the synthesis of metal NPs.

The extraction and isolation of nanocellulose from biomass involve some vigorous pre-treatment processes,¹⁵ directing the elimination of non-cellulosic components, such as polymers of free sugar, fatty acids, flavonoids, terpenoids, hemicellulose and lignin,¹⁶ carried out in a number of chemical, mechanical, and combined methods.^{15,17} A typical approach generally involves alkali treatment with a strong base (NaOH), followed by bleaching with H₂O₂, sodium chlorite, *etc.*, and finally acid hydrolysis using strong mineral acids.¹⁷ Although the methods are effective as it is claimed, there are some serious concerns to be addressed. Conventional pre-treatments are lengthy involving more than 40% of the total processing cost and energy consumption.¹⁸ Also, the use of harsh chemicals for cellulose extraction is not considered as “green”, negatively interrupting the process through the generation of toxic and hazardous waste, material contamination, degradation, and overall environmental stress.¹⁵ Recently, a variety of advanced methods such as ionic liquid treatments,¹⁹ use of deep eutectic solvents,²⁰ microwave²¹ and ultrasonic treatments,²² have also been explored. In this regard, the development of a simple extraction method to isolate cellulose fibers from waste fruit peels without using sophisticated chemical pre-treatments or techniques is in line with environmental preservations and sustainability.

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Pd(0)-embedded-lignocellulosic nanomaterials: A bio-tailored reusable catalyst for selective C2–H arylation of free N–H indoles

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ABSTRACT

Lignocellulose—a carbon-neutral renewable source has been utilized as a convenient support material for Pd nanoparticles, without disturbing its natural bio-structure. Herein, we demonstrated a green and rapid assessment of lignocellulosic nanomaterials derived from waste fibrous-feedstock of pomegranate peels using a simple extraction process in aqueous medium. The formation of lignocellulose bio-support has been authenticated by standard spectroscopic analyses. The newly developed features of Pd bio-nanomaterials were exhibited towards directing-group-free catalytic C2–H arylation of indoles with arylboronic acids. Access to vital C2-arylated indoles (62–91%) were achieved with high regioselectivity, reusability for at least five reaction cycles and admirable functionality tolerance of free N–H indole moieties. Further applicability of the catalyst was noted for selective double-functionalization of indole frameworks in a one-pot system.

1. Introduction

The fusion of nanoparticle technology and nano-porous materials is prominently one of the most intriguing and advancing areas of research (White et al., 2009; Knossalla et al., 2018). Anchoring and immobilization in a solid support allows fine-tailoring and control over shape, size, and activity of nanoparticles, along with the generation of well dispersed specific adsorption sites (Pacchioni and Freund, 2018; Ndolomingo et al., 2020). Although the concept of supported metal nanoparticles has always excited the scientific community. Last decade has witnessed innumerable potential in biomass and biomass-derived materials as promising candidates (Deplanche et al., 2014; Shah et al., 2021; Kunwar et al., 2017). Being the nature's most abundant bio-renewable and sustainable source of organic carbon, lignocellulosic biomass has gained enormous importance due to their wide availability, easy accessibility, high adsorption ability and eco-friendly characters (Akhtar et al., 2020).

Structural framework of lignocellulosic biomass is mainly composed of three bio-polymers— cellulose, hemicellulose and lignin (Isikgor and Becer, 2015), organized in complex non-uniform 3D structures varying to different degrees and relative composition depending on the bio-precursor (Yan et al., 2020). Its unique structural features and versatility hold enormous prospective for employing it as a suitable support material for metal nanoparticles (Akhtar et al., 2020; Sohni et al., 2018). Much of the current research is

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Molecular-iodine catalyzed selective construction of cyclopenta[*b*]indoles from indoles and acetone: a green gateway to indole-fused cycles†

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Molecular-iodine catalyzed access to an important class of bio-relevant indole derivatives, cyclopenta[*b*]indoles, has been achieved *via* a cascade addition/intramolecular cyclization reaction of indoles and acetone. Explorations of diverse substitution patterns revealed an essential substrate-control in the reaction. The high-density electronic core of indole is pivotal in favouring the formation of indolyl-cyclopenta[*b*]indole derivatives; in contrast, the electron deficiency of the core hindered the cyclization process, directing the formation of bis(indolyl)propanes. Investigations on the mechanistic pathway revealed that bis(indolyl)alkanes were the intermediates for the addition–cyclization process. This simple experimental method provides sustainable synthetic access to cyclopentannulated indoles.

Introduction

Indole-fused annulated structures form an important class of privileged nitrogen-heterocycles due to their widespread occurrence in natural products and active pharmaceutical ingredients.^{1–4} Among them, cyclopentannulated indoles are especially attractive because of their prevalence in numerous alkaloids, presenting impressive pharmacological activities including cytotoxicity, antibacterial and insecticidal properties, and acting as enzyme receptors.^{5–7} Their enormous biological significance has prompted researchers to contribute to the design and construction of these natural product-inspired frameworks and drug-like molecules.

In the past decade, various approaches have been developed to assemble cyclopenta[*b*]indole structural motifs.^{8,9} Some of the prominent approaches were based on [3 + 2]-cycloaddition,^{10–12} Nazarov cyclization,^{13,14} Michael addition/Friedel–Crafts process,^{15,16} and various acid-promoted^{17–19} and transition metal-mediated cyclization processes.^{20–23} However, the majority of the processes relied on pre-functionalized aniline or indole derivatives, requiring specialized designing and multistep preparation of the starting com-

pounds.²⁴ Hence, the quest for a simple process from readily available starting materials is highly desirable.

The simplest access to this class of indole derivatives is *via* using indoles and ketones as the starting materials. The initial synthesis of cyclopenta[*b*]indole by reacting indole and acetone under strong acidic conditions of ethanolic HCl or trifluoroacetic acid and its structural determination were reported in 1989 by Bergman *et al.*²⁵ Subsequently, a few studies using mineral and Lewis acidic conditions were disclosed.^{26–28} However, most of the reaction conditions are toxic and corrosive in nature, causing handling and disposal problems. Also, the reaction between indole and acetone under strong acidic conditions has proved to be complex in nature due to the possibility of the formation of a wide variety of products.^{25,28,29} Recently, two research groups, namely Nadkarni *et al.* and Shelke *et al.*, reported the use of Bi(NO₃)₃·5H₂O-zirconia³⁰ and Bi(OTf)₃,³¹ respectively, as catalysts for the transformation. However, limited substrate explorations and the hygroscopic nature of the catalysts restrict their practical utility on a large scale. Thus, knowledge of the reactions between ketones and substituted indoles to synthesize cyclopenta[*b*]indoles is still limited and they deserve exploration.

In the present times, molecular iodine-catalysis has emerged as a versatile tool in various organic transformations.^{32,33} Its marvellous catalytic activeness combined with its economical and environment-friendly attributes makes it an attractive choice for synthetic chemists.³⁴ Bandgar *et al.* have shown one example of an iodine-catalyzed reaction between indole and acetone forming bis(indolyl)methane.³⁵ However, no account of its catalytic feasibility towards cyclopenta[*b*]indole synthesis has been disclosed so far. In the

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REVIEW



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Organocatalytic dimensions to the C–H functionalization of the carbocyclic core in indoles: a review update

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An integration of two dynamic research paradigms – organocatalysis and remote C–H bond functionalization – has emerged as a profound competitor to conventional transition-metal catalyzed processes. In the contemporary research world of ample metal mediated transformations, there is a unique space for organocatalytic functionalization techniques. The benzene core in indoles remains difficult to explore owing to the dominant reactivity of the pyrrole core. Yet, exciting developments have been achieved to access remote regioselectivities: the C4, C5, C6 and C7 positions. This review documents contributions devoted to the metal-free organocatalytic functionalization of indoles in the carbocyclic ring positions up to the middle of 2020.

1. Introduction

The synthesis and functionalization of the privileged structural motif of the indole heteroaromatic system has engaged a lot of attention in the scientific community over the past century.¹ The indole core, an important module in the drug and pharmaceutical world and prevailing to its large manifestation in natural and synthetic compounds, has been recognized as a

“privileged structure”.² Basically, the construction of substituted indole derivatives was achieved by two main synthetic paradigms: (a) construction of the indole ring system from pre-designed starting molecules,³ and (b) direct functionalization of existing indole frameworks,⁴ resulting in the multitude of synthetic methods that are available in the literature.⁵ Structurally, there are six C–H bonds and one N–H bond in the indole motif available for direct C–H activation and functionalization: positions N1, C2 and C3 in the pyrrole core, and C4–C7 in the benzene core. However, all these C–H bonds are non-equivalent in terms of reactivity and electronic pro-

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Utpal Bora

Dr Utpal Bora received his Ph.D. in 2005 under the guidance of Dr R. C. Boruah at CSIR-NEIST Jorhat. He was a recipient of a JSPS postdoctoral fellowship to work with Professor Hironao Sajiki at Gifu Pharmaceutical University, Gifu, Japan during 2005–07. In 2008, he joined Syngene International Limited, Bangalore as Associate Scientific manager and later moved to the Department of Chemistry, Dibrugarh University, Dibrugarh as Assistant Professor in 2008. In 2013 he joined the Department of Chemical Sciences, Tezpur University, Tezpur, where he is currently working as an Associate Professor. His research interests include catalysis, organic synthesis, and C–H activation.