

## Annexure-B

### List of Publications

1. **Kataky, S.**, Sarma, B., and Thakur, A. J. Preparation of 2, 5-Disubstituted Tetrazoles using a Copper-Catalysed Regioselective Direct Coupling of Tetrazoles with Free NH Groups and Boronic Acid Derivatives. *ChemistrySelect*, 8(42):e202301843, 2023.
2. **Kataky, S.**, Boruah, P., and Thakur, A. J. Lewis Acid Catalysed Chemoselective Amination of Alcohols Using Heterocyclic Thiones: An Avenue to Thiotetrazole Derivatives. *European Journal of Organic Chemistry*, e202300515, 2023.
3. Bhuyan, P., Bhorali, P., **Kataky, S.**, Bharali, S. J., Guha, A. K., and Saikia, L. ZnCl<sub>2</sub> catalyzed cascade conjugative alkynylation/6-endo-dig cyclisation of N,N-dimethyl barbituric acid derived alkenes under ultrasonic irradiation: An improved, base & column-free access to pyrano[2,3-*d*]pyrimidine-2,4(3*H*,5*H*)-diones. *Sustainable Chemistry and Pharmacy*, 30:100852, 2022.
4. Ligand free CuO nanoparticles catalysed S-arylation of heterocyclic thiols using aryl halides. Authored by **Sudhamoyee Kataky**, Sultana Parveen Ahmed, Ankita Rakshit and Prof. Ashim Jyoti Thakur (*under communication*).
5. Pd nanoparticles supported on luffa sponge as a heterogenous catalyst for C-O and C-C coupling reaction: From waste to use. Authored by **Sudhamoyee Kataky**, Bhavna Choudhury, Gayatri Neog, Manash R. Das and Prof. Ashim Jyoti Thakur (*under communication*).

### Conference attended

1. National Seminar On “Research at The Interface Of Chemical, Biological And Material Sciences” organised by Department of Chemical Sciences in collaboration with Students’ Science Council, Tezpur University, March 10, 2023.

2. International Conference On "Interface of Chemistry, Material Chemistry and Pharmaceutical Sciences" organised by Department of Chemistry, Royal School of Pharmacy, Royal Global university and Department of Chemistry, Cotton University, November 10, 2023.



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The following ALERTS were generated. Each ALERT has the format

**test-name\_ALERT\_alert-type\_alert-level.**

Click on the hyperlinks for more details of the test.

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 **Alert level B**

PLAT306\_ALERT\_2\_B Isolated Oxygen Atom (H-atoms Missing ?) ..... 02 Check

**Author Response: Hydrogen atoms of the coordinated water molecule were not located. Presence of heavy metal atom provides uncertainty in the position of hydrogens like OH, NH, but are included in the formula.**

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 **Alert level C**

PLAT088\_ALERT\_3\_C Poor Data / Parameter Ratio ..... 9.10 Note  
PLAT230\_ALERT\_2\_C Hirshfeld Test Diff for N4 --C1 . 6.5 s.u.  
PLAT232\_ALERT\_2\_C Hirshfeld Test Diff (M-X) Cu1 --N2 . 5.8 s.u.  
PLAT234\_ALERT\_4\_C Large Hirshfeld Difference N4 --C13A . 0.18 Ang.  
PLAT911\_ALERT\_3\_C Missing FCF Refl Between Thmin & STh/L= 0.594 49 Report

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 **Alert level G**

PLAT066\_ALERT\_1\_G Predicted and Reported Tmin&Tmax Range Identical ? Check  
PLAT083\_ALERT\_2\_G SHELXL Second Parameter in WGHT Unusually Large 27.72 Why ?  
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PLAT232\_ALERT\_2\_G Hirshfeld Test Diff (M-X) Cu1 --C11 . 49.2 s.u.  
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PLAT300_ALERT_4_G	Atom Site Occupancy of H16D	Constrained at	0.5	Check
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	$-1/3+y, 1/3-x+y, 1/3-z =$		14_455	Check
PLAT432_ALERT_2_G	Short Inter X...Y Contact C3B ..C4A	.	2.96	Ang.
	$2/3+x-y, 1/3+x, 1/3-z =$		15_555	Check
PLAT432_ALERT_2_G	Short Inter X...Y Contact C5A ..C11B	.	3.20	Ang.
	$2/3+x-y, 1/3+x, 1/3-z =$		15_555	Check
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	$4/3-y, 2/3+x-y, -1/3+z =$		8_654	Check
PLAT432_ALERT_2_G	Short Inter X...Y Contact C6A ..C11B	.	2.89	Ang.
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It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special\_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

### **Publication of your CIF in IUCr journals**

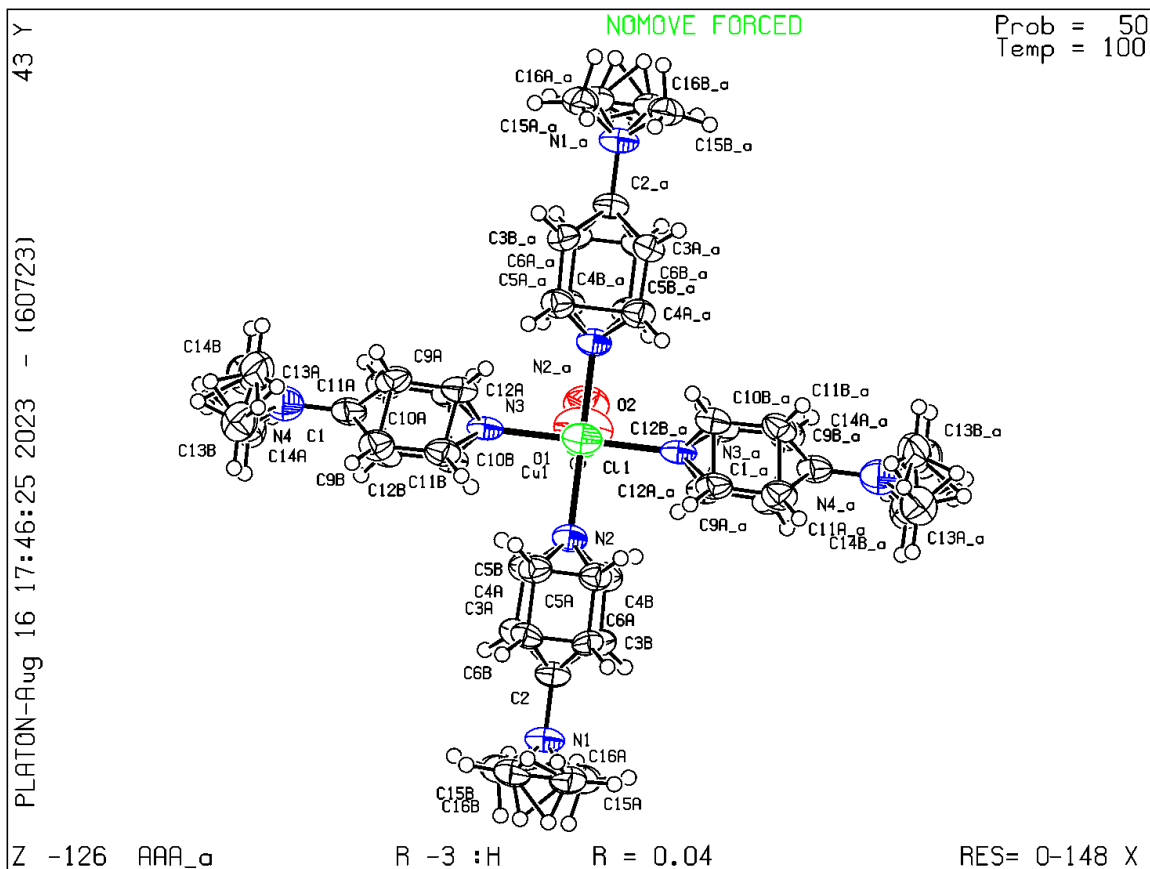
A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that **full publication checks** are run on the final version of your CIF prior to submission.

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# Preparation of 2,5-Disubstituted Tetrazoles using a Copper-Catalysed Regioselective Direct Coupling of Tetrazoles with Free NH Groups and Boronic Acid Derivatives

Sudhamoyee Katakya,<sup>[a]</sup> Bipul Sarma,<sup>[a]</sup> and Ashim Jyoti Thakur<sup>\*[a]</sup>

The development of a mild and efficient protocol that allows the direct C–N coupling of N–H free tetrazole and low toxic boronic acid was presented. A careful optimization of the reaction conditions revealed that reaction proceeded smoothly

in presence of a 10 mol% copper complex catalytic system without the need of any additives. Thus, the results presented herein represents a reliable and efficient protocol for the synthesis of regioselective 2,5-disubstituted tetrazoles.

## Introduction

Amongst the various nitrogen-containing heterocycles, scaffolds based on tetrazole offer a plethora of applications in the domain of medicinal chemistry, coordination chemistry, material sciences, high energy materials, biochemistry, pharmacology, and agriculture (as herbicides and fungicides).<sup>[1–5]</sup> Notably, they have the highest number of nitrogen atoms among the stable *N*-heterocycles and have been widely considered as a suitable precursor to various important scaffolds.<sup>[6–10]</sup> Recent studies have shown that there has been renewed interest in the preparation of tetrazoles as a substantial number of active pharmaceutical ingredients (API) contain the tetrazole ring.<sup>[11–14]</sup> For instance, numerous pharmacological applications of tetrazoles are anti-inflammatory, antihypertensive, anticancer, anti-allergic, antibiotic, diuretics and receptor modulatory agents.<sup>[7,15,16]</sup> Losartan, an important drug of the sartan family and an FDA approved antihypertensive drug is a 5-aryl-1*H*-tetrazole, while Candesartan Cilexetil which is an angiotensin II receptor blocker (ARB) is also a 5-aryl-1*H*-tetrazole (Figure 1).<sup>[17,18]</sup> Tetrazole derivatives such as 1,5- and 2,5-disubstituted tetrazoles are used as carboxylic acid isosteres and amide isosteres (Figure 1) respectively which play important roles in enhancement of lipophilicity, bioavailability, pharmacokinetic properties and side effect reduction of the drug molecules.<sup>[1,19,20]</sup> Furthermore, both 1,5- and 2,5-disubstituted tetrazoles also find use in coordination chemistry, as a stabiliser in photographic industry, or as components of special explosives.<sup>[2,21]</sup> In particular, 2,5-disubstituted tetrazoles are often used as pharmacophores and photosensitive materials and a convenient precursor for the preparation of a variety of *N*-heterocycles.<sup>[22–24]</sup>

Despite its numerous uses, there are only few synthetic methodologies developed so far for *N*-arylation of tetrazoles with aryl boronic acids. The traditional approach to access 2-aryl-5-substituted tetrazoles was *via* Kakehi methodology, where potentially explosive aryl diazonium salts and phenyltosylhydrazones were used.<sup>[21]</sup> With a wide variety of commercially available phenyl boronic acids and their derivatives, the Chan-Lam reaction has emerged as an efficient and valuable alternative to the traditional cross-couplings in the formation of carbon–heteroatom bonds.<sup>[25–29]</sup>

Lam and co-workers used stoichiometric amount of Cu(OAc)<sub>2</sub> for reaction between 5-phenyltetrazole and *p*-tolylboronic acid that required longer reaction time (Scheme 1).<sup>[30,31]</sup> Moreover, when diaryliodonium salts were used as the coupling partner to generate 2,5-disubstituted tetrazoles, such methods were not only operationally tedious, but also generated stoichiometric amounts of the respective aryl iodide.<sup>[23]</sup> Another route for *N*<sup>2</sup>-arylation used arylbismuth as the arylating source under copper catalysis.<sup>[32]</sup> Other multi-step procedures based on various cyclization protocols for the synthesis of 2,5-disubstituted tetrazole derivatives have also been reported. Han and co-workers recently reported the synthesis of 2-aryl-5-substituted tetrazoles through the coupling of 5-substituted 1*H*-tetrazole with arylboronic acid in the presence of a catalytic amount of copper(II) oxide at 100 °C (Scheme 1).<sup>[31,32]</sup> This *N*-arylation approach was revisited by Maegawa and co-workers where they applied a catalytic amount of [Cu(OH)(TMEDA)]<sub>2</sub>Cl<sub>2</sub> in an O<sub>2</sub> atmosphere at room temperature for 16 hours (Scheme 1).<sup>[33]</sup> The reaction was not regioselective under Han's condition as it yielded a mixture of two regio-isomers i.e. 2-phenyl and 1-phenyl-5-methyltetrazoles. The formation of the product mixture can be due to the existence of two isomeric forms.<sup>[31]</sup> Therefore, the selective arylation of tetrazole is a difficult process as it gives rise to a mixture of regioisomeric products. On the contrary, Maegawa's protocol was highly regioselective, and various functionalized tetrazoles were exemplified. In addition to that a "suitable steric environment" of TMEDA was credited for such selectivity.<sup>[33]</sup> We report herein a simple and robust copper complex catalytic system for *N*<sup>2</sup>-arylation of tetrazoles with arylboronic acids.

[a] S. Katakya, Prof. Dr. B. Sarma, Prof. Dr. A. J. Thakur  
 Department of Chemical Sciences, Tezpur University, Tezpur, Napaam-784028, India  
 E-mail: ashim@tezu.ernet.in  
 Homepage: <https://www.tezu.ernet.in/dcs/faculty/11>

Supporting information for this article is available on the WWW under <https://doi.org/10.1002/slct.202301843>

# Lewis Acid Catalysed Chemoselective Amination of Alcohols Using Heterocyclic Thiones: An Avenue to Thiotetrazole Derivatives

Sudhamoyee Katakya,<sup>[a]</sup> Pikumoni Boruah,<sup>[a]</sup> and Ashim J. Thakur\*<sup>[a]</sup>

Herein, a protocol for the chemoselective formation of C–N bond using Cu(OTf)<sub>2</sub> as catalyst has been described using heterocyclic thiones. The reaction occurs preferentially at the nitrogen centre over the sulphur atom leading to C–N bond formation. Water being the only by-product, the reaction is environmentally friendly. The reaction proceeds without any

additive, ligand or inert atmosphere and shows good tolerance towards variety of alcohols and thiotetrazole derivatives. Our developed protocol could be scaled up to gram scale efficiently, which highlights the efficacy of this method and might offer potential application in synthetic industry.

## Introduction

Sulphur containing heterocycles exist in various naturally occurring compounds and exhibit many pharmacological activities like anticancer, antiviral, anti-inflammatory, antimicrobial, and antitubercular.<sup>[1,2]</sup> For instance, thiotetrazoles are sulphur-based heterocyclic compounds which contain S- and N-atoms possessing a wide variety of biological activities including anti-viral and anti-inflammatory properties.<sup>[3–5]</sup> Moreover, they are useful precursors for C–S and C–N bond-formation. However, utility to form C–N bond is rare.<sup>[6–8]</sup> It is well known to function both as sulphur and nitrogen nucleophiles.<sup>[9]</sup> Owing to ambident nucleophilic nature of thiotetrazoles, the development of chemoselective amination is a difficult task. Recently, direct dehydrative nucleophilic substitutions using free alcohols as substrates catalysed by Lewis and Brønsted acids have attracted much attention in organic synthesis.<sup>[10–13]</sup> Because of the general availability, low cost and water being the only by-product produced, alcohols are regarded as the best arylating partner compared to other arylating agents such as aryl halides.<sup>[14–18]</sup> Prior conversion of alcohols to good leaving group was of no use in this dehydrative substitution strategy, thereby eliminating multi-step procedures, wastages of fine chemicals and helps further to achieve atomically efficient method.<sup>[19,20]</sup> In contemporary organic synthesis, Lewis acid catalysed reactions have gained increasing popularity because of the unique reactivity and selectivity that can be easily achievable under mild reaction conditions.<sup>[21–24]</sup> We speculated that a similar approach may enable direct alcohol arylation as Lewis acid catalyst provides powerful strategy to facilitate activation and

derivatisation of alcohols *via* an S<sub>N</sub><sup>1</sup> and S<sub>N</sub><sup>2</sup> type pathway.<sup>[25–27]</sup> To our surprise, a limited number of Lewis acid promoted selective amination and sulfonylation of alcohols with thiotetrazoles are developed. Our on-going studies on mild and efficient synthetic methods for producing chemo selective aminated product led to potentially examine more convenient and safe catalysts.<sup>[28]</sup> Ease of handling, accessibility, enhanced reaction rates, greater selectivity and inherent stability in aqueous solvents copper(II) triflate was best regarded as Lewis acid catalyst.<sup>[29]</sup> Cu(OTf)<sub>2</sub> has long been known to promote elimination reactions, oxidative coupling reactions and reactions of diazo compounds.<sup>[30,31]</sup> Our findings provide a general, complementary approach and represent underexplored examples under mild reaction conditions. The use of environmentally benign, readily accessible substrates and catalysts provides a greener approach to chemoselective aminated product.<sup>[32–35]</sup>

Recently, a few distinct strategies have been explored for C–N and C–S bond formation using acid catalyst. As a pioneering work, Wu's group<sup>[2]</sup> has reported sulfonylation protocol of alcohols catalysed by Ga(OTf)<sub>3</sub>. However, the scope of this reaction was limited to S-arylated dehydrative substitution of alcohols (Scheme 1(1a)). In 2018, Prabhu *et al.* disclosed a novel method for the chemoselective amination<sup>[4]</sup> of alcohols using iodine as catalyst. However, the scope of this protocol is limited to 1-methyl-1*H*-tetrazole-5-thiol where reactions with 1-phenyl-1*H*-tetrazole-5-thiol were discussed only with cinnamyl alcohol (Scheme 1(1b)). It was also seen that the reaction of primary alcohol with 1-methyl-1*H*-tetrazole-5-thiol under iodine catalysed condition delivered inseparable mixture of products. In our reaction, we obtained chemoselective aminated product exclusively by reacting both phenyl and methyl substituted thiotetrazoles with varied alcohol derivatives. With an intention to design robust methodology we attempted to work with aromatic as well as aliphatic alcohols. Successful amination of *tert*-butyl group with thiotetrazoles which was unexplored in previous methodologies yield excellent results under our protocol. Restricting to only secondary alcohols, very recently Nakata's group<sup>[9]</sup> has reported both N- and S- arylation in

[a] S. Katakya, P. Boruah, Prof. Dr. A. J. Thakur  
Department of Chemical Sciences  
Tezpur University  
Napaam 784028, Assam (India)  
E-mail: ashim@tezu.ernet.in

Supporting information for this article is available on the WWW under <https://doi.org/10.1002/ejoc.202300515>