4.1 Introduction

4.1.1 Importance of organosulphur compounds

The development and application of cross-coupling reactions has an immense impact in the field of organic chemistry. The products of such transformations are often used as pharmaceuticals, fine chemicals, dyes and polymers [1,2]. In particular, C–S bond forming reactions have gained much attention since thioethers are of significant importance due to their vast spectrum of therapeutic activities [3-5]. Approximately, 20% of all drugs approved by the Food and drug administration (FDA) constitute organosulphur compounds. They are present in important biological and pharmaceutical products, such as nelfinavir (antiretroviral), vortioxethine (antidepressants), Latamoxef (antibiotic), and Cefpiramide (antibacterial) [6,7] (Figure **4.1**). For instance sulphur heterocycles, specifically tetrazole-5-thione rings are featured in many antiviral, antibacterial, analgesic, anaesthetic, antihistaminic, antimicrobial, anti-inflammatory and anticancer drugs [8,9].

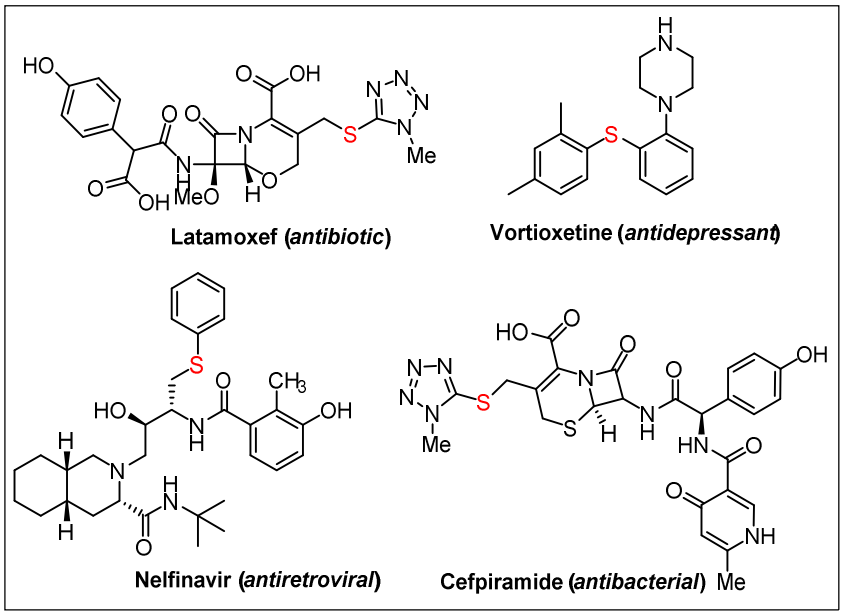


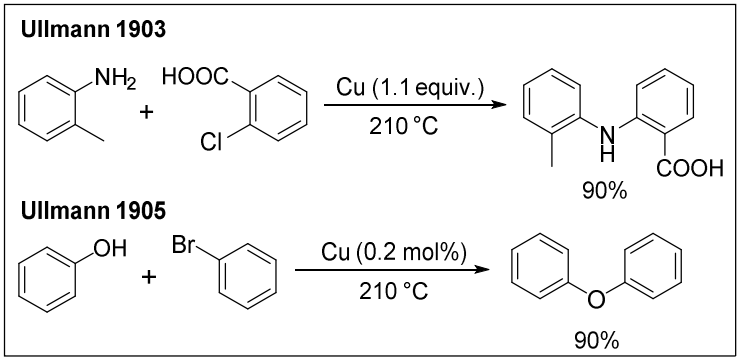
Figure **4.1** Important drug molecules containing sulphur

Among the subclasses of substituted tetrazole-5-thiols, 1-alkyl-5-arylthiotetrazoles have been explicitly studied for their potential antibiotic, anti-viral and anti-inflammatory properties [10,11]. Apart from having pharmaceutical activities, sulphur-containing heterocyclic motifs also find potential applications in

agriculture and material sciences [12,13]. Therefore, demand for organosulphur compounds increases constantly, demanding safer, cleaner and cheaper methodologies for syntheses [14].

4.1.2 C–S cross-coupling reaction

Copper (Cu) catalysed arylation reactions devoted to the formation of Carbon–Carbon (C–C) and Carbon–heteroatom (C-X) bonds or Ullmann coupling have acquired great significance in this area of research [15]. Aryl halides are generally the preferred electrophilic partners in Ullmann couplings. In 1903 and 1905, Ullmann had synthesized *N*-aryl amines and ethers using stoichiometric Cu and became one of the most favoured catalytic reactions in organic synthesis (Scheme **4.1**) [16,17]. Since organosulphur compounds exhibit a strong tendency to coordinate to transition metals such as palladium, leading to catalyst poisoning and consequently decrease catalyst's efficiency, thus the design of suitable catalyst avoiding these drawbacks is fundamental to get good results. Most importantly, copper catalysed C-S cross-coupling is the most preferred one compared to other transition metal catalysts [18,19].



Scheme **4.1** Schematic representation of Ullmann Coupling reactions

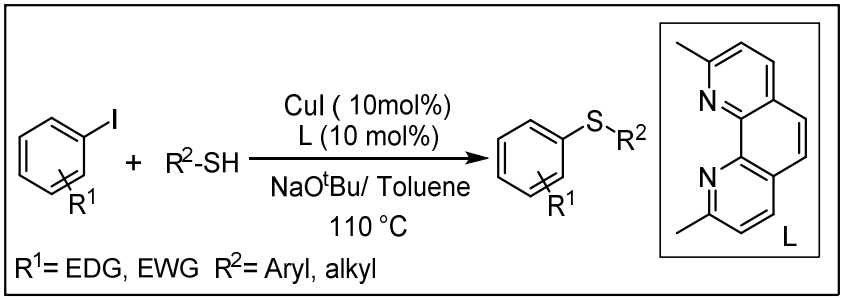
4.2 Background of the present work

4.2.1 Copper- ligand complex catalysed *S*-arylation

Cu is a 3d transition metal having interesting physical and chemical properties. Cu's wide range of accessible oxidation states (Cu^0, Cu^I, Cu^{II}, and Cu^{III}) helps promote a variety of reactions which enable reactivity *via* both one and two electron pathways [20]. Due to its unique characteristics and properties, Cu-based catalysis has found

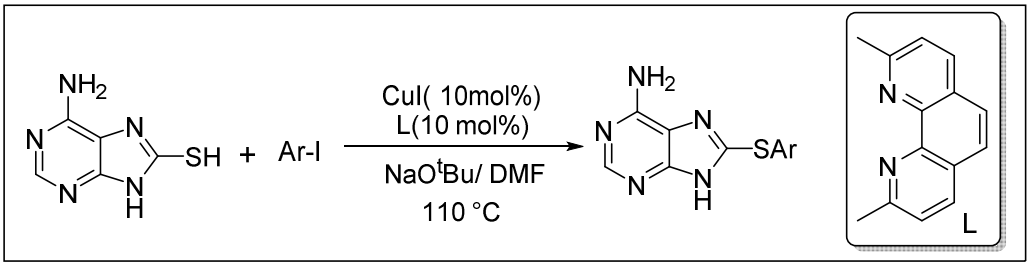
applications in nanotechnology, organic transformations, electrocatalysis and photocatalysis. Under mild reaction conditions, a large number of Cu salts or Cu complexes have been seen promoting *S*-arylation and alkylation reactions [21].

Venkataraman et al., have used CuI-neocuproine (2,9-dimethyl-1,10-phenanthroline) complex for the coupling of aryl and alkyl thiols with aryl iodides in presence of NaO^{t}Bu in toluene at 110 °C, affording the products in excellent yields (Scheme **4.2**) [22].



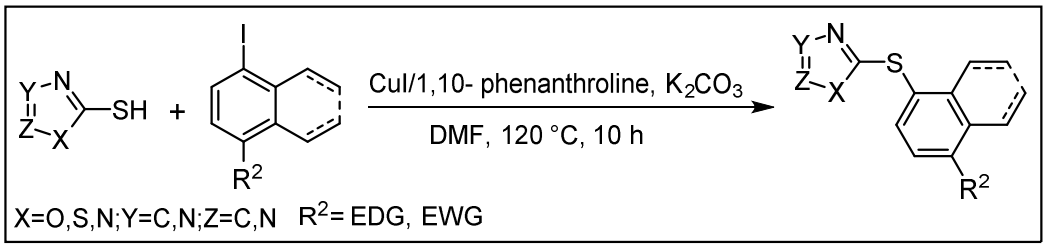
Scheme **4.2** CuI-neocuproine catalysed arylation of thiols

Chiosis et al., used the same CuI-neocuproine system for *S*-arylation of 8-mercaptoadenine with aryl iodides in DMF at 110 °C (Scheme **4.3**) [23].



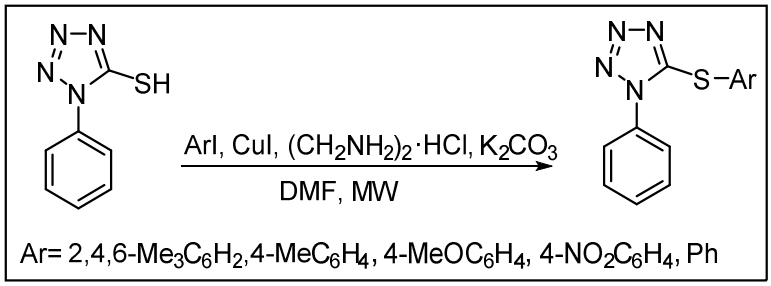
Scheme **4.3** CuI-neocuproine system for *S*-arylation of 8-mercaptoadenine

A copper-catalysed cross-coupling of heterocyclic thiols with aryl iodides was reported by Niu et al., The reaction was carried out in presence of CuI/1,10-phenanthroline as catalyst and K_2CO_3 as base in DMF at 120 °C, affording heterocyclic sulfides in high selectivity and yields (Scheme **4.4**) [24].



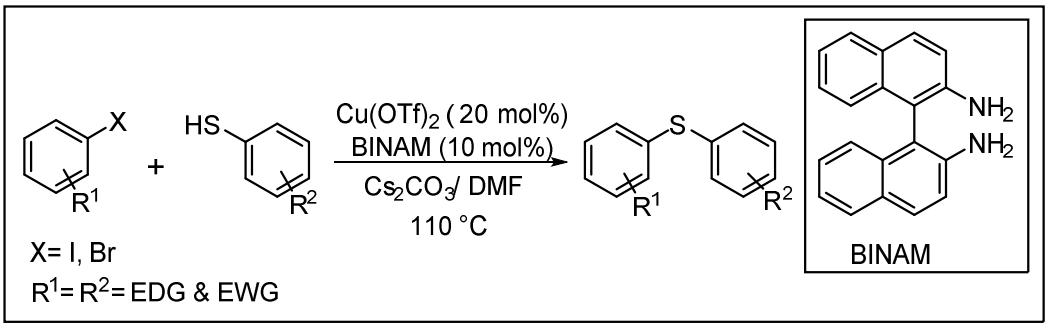
Scheme **4.4** CuI/1,10-phenanthroline catalysed *S*- arylation of heterocyclic thiols with aryl iodides

Similarly, in 2012, Myznikov and his group had carried out arylation of 1-phenyl-5-mercaptotetrazole with iodobenzene catalysed by CuI/1,2- $NH_2CH_2CH_2NH_2$ and Cs_2CO_3 as the base under microwave activation of 100 W (Scheme **4.5**) [25].



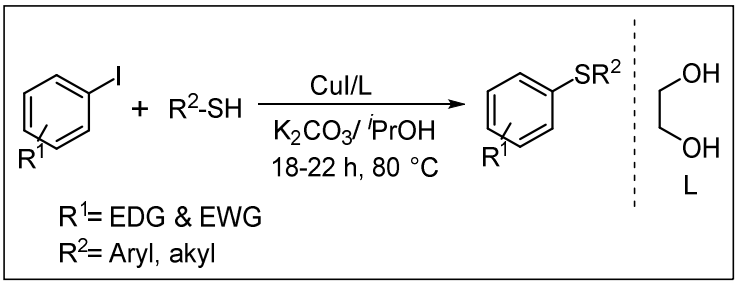
Scheme **4.5** CuI/1,2-$NH_2CH_2CH_2NH_2$ catalysed arylation of 1-phenyl-5-mercaptotetrazole with iodobenzene

Sekar et al., synthesized diarylthioethers from thiols and aryliodides in presence of $Cu(OTf)_2$/BINAM complex and Cs_2CO_3 in DMF at 110 °C. Notably the reaction yields were unaffected by the position of substituents on the aryl iodide (Scheme **4.6**) [26].



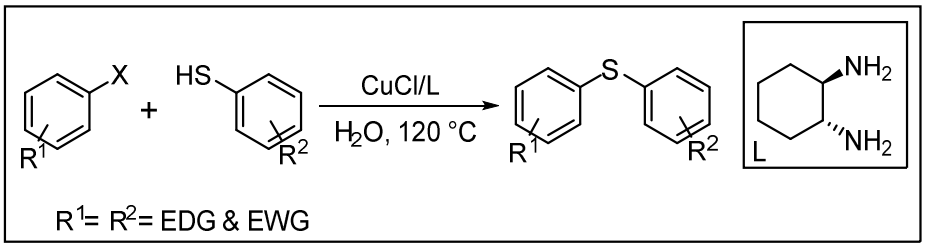
Scheme **4.6** $Cu(OTf)_2$/BINAM complex catalysed arylation of thiols

Buchwald and Kwong reported a simple thioether formation protocol from aryl iodides and aryl/alkyl thiols using CuI/ethyleneglycol and K_2CO_3 in isopropanol at 80 °C (Scheme **4.7**) [27].



Scheme **4.7** Arylation of thiols using CuI/ethyleneglycol

An environmentally benign diarylthioether coupling in water was reported by Carril and group. Under the optimized reaction conditions, aryl thiol and aryl iodide or aryl bromide were heated in water at 120 °C in the presence of CuCl and *trans*-1,2-diaminocyclohexane. Electron-donating and electron-withdrawing as well as free –NH and –OH on the aryl iodide partner and aryl thiol partner were found to be compatible with the reaction conditions (Scheme **4.8**) [28].

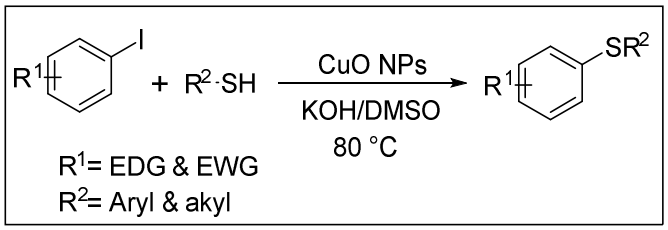


Scheme **4.8** Arylation of thiols using CuCl/ trans-1,2-diaminocyclohexane

4.2.2 Cu nanoparticles catalysed *S*-arylation

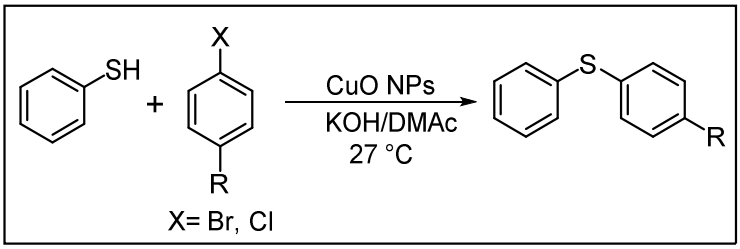
The wide applications of copper based NPs have generated a great deal of interest in recent years, especially in the field of catalysis [29,30]. The most significant benefits of employing CuO NPs in a reaction is its commercial availability and relatively low toxicity compared to precious metal-based NPs, possibility to carry out reactions under ligand-free conditions and catalyst recyclability [29,31]. Some of the important C-S bond formation reactions catalysed by CuO NPs are discussed below:

Punniyamurthy and his group developed ligand-free CuO NPs catalysed C-S cross-coupling of aryl and alkyl thiols with aryl iodides in presence of 1.26 mol% of the catalyst in DMSO at 80 °C affording good yield of the products in less than 10 hours (Scheme **4.9**) [31].



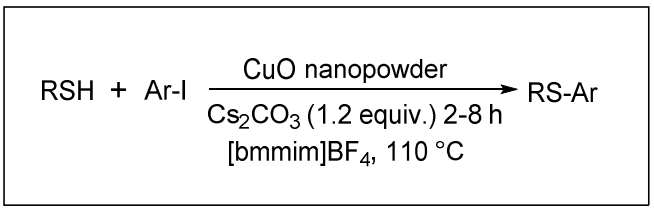
Scheme **4.9** CuO NPs catalysed C-S cross-coupling of aryl and alkyl thiols with aryl halides

Babu and Karvembu reported ligand-free CuO NPs catalysed C-S cross-coupling of aryl halides with thiophenol in presence of KOH as base in dimethylacetamide (DMAc) at room temperature (Scheme **4.10**)[32].



Scheme **4.10** CuO NPs catalysed C-S cross-coupling of aryl halides with thiophenol

Another CuO NPs catalysed cross-coupling reaction of thiols with aryl iodides in [bmmim]BF_4 was reported by Braga et al. Compared to the usual organic solvents, [bmmim]BF_4 exhibited more efficiency as it can be reused up to four successive runs (Scheme **4.11**) [33].

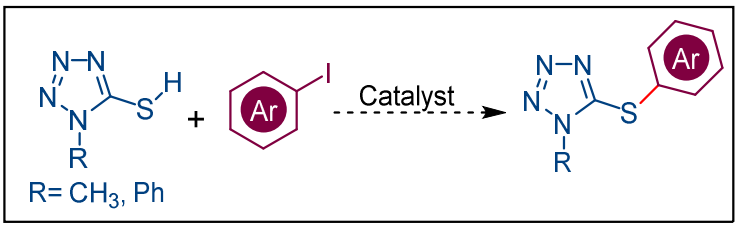


Scheme **4.11** CuO NPs catalysed cross-coupling reaction of thiols with aryl iodides in [bmmim]BF_4

4.3 Objectives of the present work

One of the most common synthetic methodologies for the preparation of C–S bond is the conventional copper-catalysed Ullmann coupling [34,35]. Most of the systems involve a homogeneous catalyst and the ligand chelated with the metal that plays a crucial role in catalysis. Nevertheless, these reactions often require harsh conditions such as high temperature, stoichiometric amount of metal catalyst, which on scaling-up leads to waste generation [36]. Encouraged by the crucial advantages of CuO NPs such as high atom efficiency, commercial availability, possibility to carry out reactions under ligand-free conditions, easy recovery and recyclability; we decided to study the scope of CuO NPs for C–S cross-coupling reactions of thiotetrazoles [37].

Heterocyclic thiols serve as important building blocks for synthesizing a variety of pharmaceutically and medicinally active sulphur containing compounds. Interestingly, sulphur-containing organic transformations can be more easily accomplished with Cu or CuO NPs compared to Pd or other transition metals. This is because sulphur is known to have a strong affinity for Pd and deactivates the catalyst completely [31]. Thus, there is a huge demand for strategies to establish a mild and efficient synthetic methodology to provide *S*-aryl/(hetero)aryl products (Scheme **4.12**). Our present work is based on Scheme **4.12**.



Scheme **4.12** Proposed scheme for arylation of thiotetrazoles

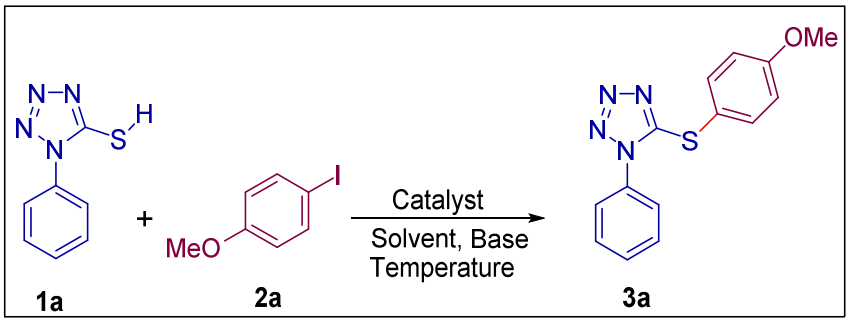
4.4 Results and Discussion

4.4.1 Optimization table

We began our investigations by using 1-phenyl-1*H*-tetrazole-5-thiol (**1a**) and 4-methoxyiodobenzene (**2a**) as model substrates (Table **4.1**). Optimization of the reaction conditions included screening of solvents, bases, catalysts, temperature, base loadings and catalyst loadings. It was found that the reaction was significantly

affected by the nature of solvent and highest yield was obtained when dimethyl formamide (DMF) was used (Table **4.1,** entry 6). Other solvents such as PEG 400, toluene, 1,4-dioxane, H_2O, ethanol were also tested but failed to deliver the desired product (Table **4.1,** entries 14-18). Subsequently, examination of base loading showed that 1.5 equiv. of K_2CO_3 was most suitable and upon increasing the amount of base to 2 equiv., no change in yield was observed (Table **4.1,** entries 5 and 6). It was also noticed that decreasing the amount of base to 1 equiv., product yield was slightly decreased (Table **4.1,** entry 7). Similarly, base screening showed that K_2CO_3 was the most suitable choice among other bases examined (Table **4.1,** entries 6 and10-12). Next, we examined the catalyst loading of CuO NPs and it was noticed that when catalyst loading was increased from 10 mol% to 15 mol% and 20 mol%, no significant change in product yield was observed (Table **4.1,** entries 1-6). Further exploration of the reaction conditions showed that upon decreasing the catalyst loading from 10 mol% to 5 mol%, a decrease in product yield was seen (Table **4.1,** entry 9). Thus, 10 mol% was the optimum amount that delivered the product in highest yield. Thereafter, the reaction was studied by taking the catalyst amount at 10 mol%. Finally, a decrease in product yield was observed upon lowering the reaction temperature from 100 °C to 80 °C; whereas upon increasing the temperature to 120 °C, made no significant difference (Table **4.1,** entries 1-7). So, we kept our reaction temperature at 100 °C to obtain maximum yield of the desired product. We also studied the reaction time and it was seen that 5 hours was the optimum time required to accomplish the reaction (Table **4.1,** entries 3 and 6). Further increasing the reaction time showed no significant change in yield. No product formation was observed in absence of CuO NPs (Table **4.1,** entry 19). Therefore, the best optimized reaction condition was fixed at CuO NPs (10 mol%), K_2CO_3, (1.5 equiv.), and DMF (3 mL) at 100 °C for 5 hours (Table **4.1,** entry 6) .

Table **4.1 Optimization of reaction conditions**[a]



Entry	Catalyst (NPs)	Amount of Catalyst (mol%)	Base (equiv.)	Solvent (mL)	Temp (°C)	Time (h)	Yield[b] (%) 3a
1	CuO	20	K_2CO_3 (2)	DMF	rt	12	nr
2	CuO	20	K_2CO_3 (2)	DMF	80	12	57
3	CuO	20	K_2CO_3 (2)	DMF	100	12	87
4	CuO	20	K_2CO_3 (2)	DMF	100	5	87
5	CuO	15	K_2CO_3 (2)	DMF	100	5	86
6	**CuO**	**10**	**K_2CO_3 (1.5)**	**DMF**	**100**	**5**	**86**
7	CuO	10	K_2CO_3 (1.5)	DMF	120	5	86
8	CuO	10	K_2CO_3 (1)	DMF	100	5	84
9	CuO	5	K_2CO_3 (1.5)	DMF	100	5	67
10	CuO	10	NEt_3 (1.5)	DMF	100	5	nr
11	CuO	10	Cs_2CO_3 (1.5)	DMF	100	5	86
12	CuO	10	KOH(1.5)	DMF	100	5	81
13	CuO	20	K_2CO_3 (1.5)	DMSO	100	5	79
14	CuO	10	K_2CO_3 (1.5)	PEG 400	100	5	nr
15	CuO	10	K_2CO_3 (1.5)	Toluene	100	5	nr
16	CuO	10	K_2CO_3 (1.5)	1,4-Dioxane	100	5	nr
17	CuO	10	K_2CO_3 (1.5)	H_2O	100	5	nr
18	CuO	10	K_2CO_3 (1.5)	ethanol	100	5	nr
19		10	K_2CO_3 (1.5)	DMF	100	5	nr

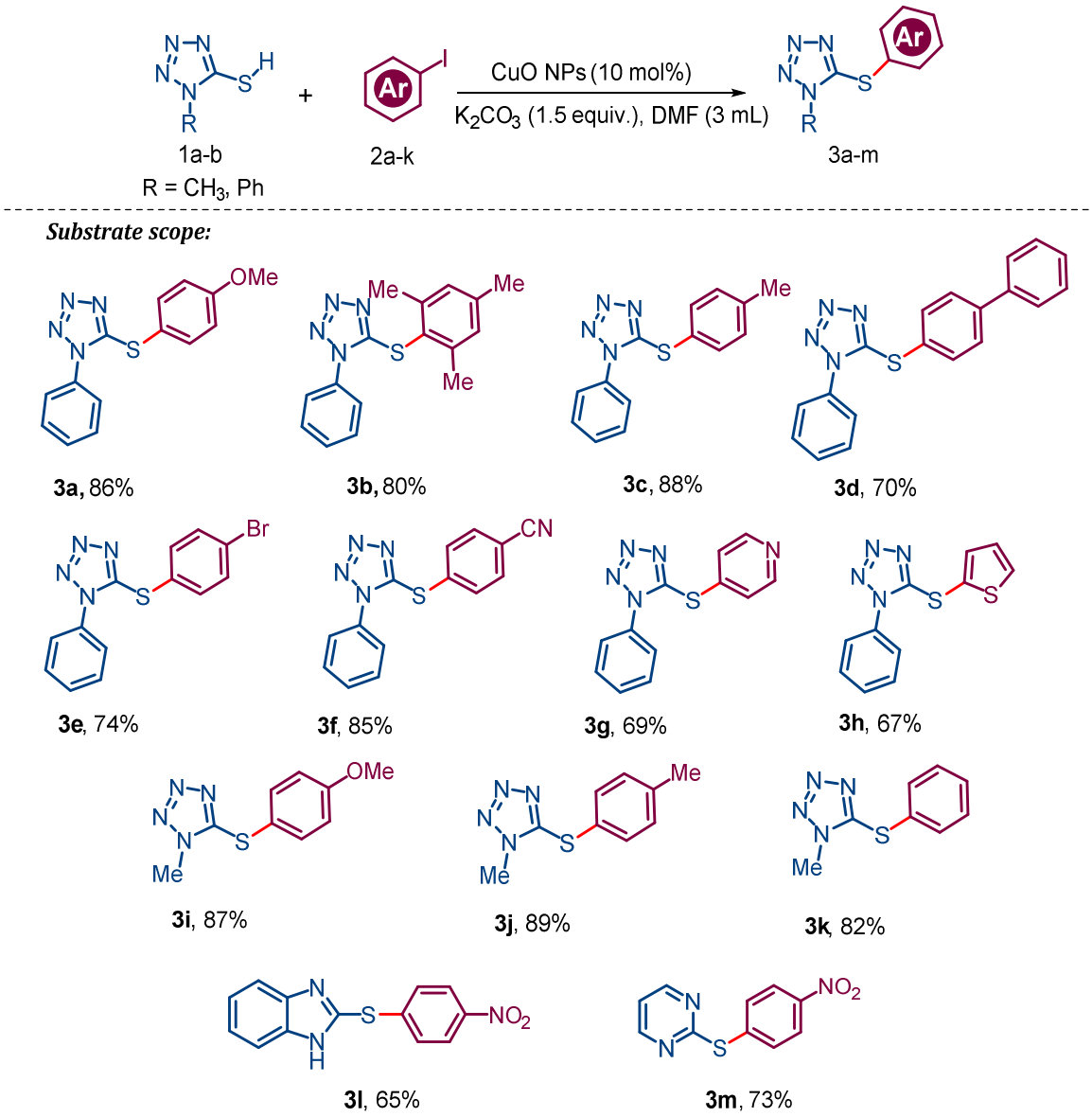
[a]*Reaction condition:* ***1a*** *(0.5 mmol),* ***2a*** *(0.65 mmol), and solvent (3 mL).* [b]*Isolated yields. nr= no reaction*

4.4.2 Substrate scope study

We next sought to study the substrate scope of the reaction using the optimized reaction conditions and the results are summarized in Table **4.2**. Initially, we

explored 1-phenyl-1*H*-tetrazole-5-thiol (**1a**) with methoxyiodobenzene (**2a**) under the optimized reaction conditions and the product (**3a**) yield obtained was excellent. Next, we tested varied derivatives of aryliodides to evaluate the effect of substituents on the aromatic ring. A range of substituted aryl iodides **(2a-k)** reacted with various derivatives of tetrazole-5-thiol **(1a-b)** giving the corresponding products in good yields.

Table **4.2 Substrate scope study**[a]



[a]*Reaction Condition:* ***1a ,b*** *(0.5 mmol),* ***2a-k*** *(0.65 mmol), DMF (3 mL),* K_2CO_3 *(1.5 equiv.) and CuO NPs (10 mol%).*

It was observed that aryl iodides bearing electron-donating groups such as –Me, -OMe (Table **4.2,** entries 3a-c) as well as electron-withdrawing groups such as -CN, -

Br transformed into their desired products with excellent yields (Table **4.2,** entries 3e-3f) respectively. We also tested the reaction of heterocyclic aryl iodides with 1-phenyl-1*H*-tetrazole-5-thiol and surprisingly both yielded moderate results (Table **4.2,** entries 3g-3h). Next, we diversified our reaction protocol towards 1-methyl-1*H*-tetrazole-5-thiol with a variety of aryl iodides such as unsubstituted aryl iodide, methoxy substituted aryl iodide, methyl substituted aryl iodides and interestingly the product yield obtained was excellent (Table **4.2,** entries 3i-3k). Under same reaction conditions, 1-phenyl-1*H*-tetrazole-5-thiol also reacted with biphenyl iodide and delivered the *S*-arylated product in good yield (Table **4.2,** entry 3d). Other heterocyclic thiols are also tried with our developed protocol and all yielded good results (Table **4.2,** entries 3l and 3m). Therefore, we are pleased to report that aryl iodides are good coupling partners to react with substituted tetrazole-5-thiol, affording the corresponding products with good to excellent yields.

4.4.3 Heterogeneity test (Hot filtration test)

To verify the heterogeneity of the catalyst hot-filtration test was performed. 10 mol% CuO NPs and K_2CO_3 in DMF (3 mL) at 100 °C were taken in a round bottomed flask. After 3h, the solid catalyst phase was filtered off using a Whatman filter paper (grade 41). In another round bottomed flask, the filtrate was collected where thiotetrazole (0.5 mmol) and 4-methoxyiodobenzene (0.65 mmol) were added wherein a negligible amount of product formation was detected after a period of 24 hours. The ICP-OES analysis of the liquid phase was recorded which revealed that the residual Cu level was less than 0.01 ppm indicating the heterogeneous behaviour of the catalyst.

4.4.4 Recyclability test

One of the salient aspects in modern catalysis research is the separation and the catalyst reusability. CuO NPs were purchased commercially from Alfa Aesar having pore diameter 30-50 nm. The catalyst is reusable, and a variety of heterocyclic thiols and iodobenzenes underwent the reaction in high yields. CuO NPs catalyst was recycled with good to moderate reactivity over three consecutive runs as shown below. However, a slight loss in reactivity was seen which can be attributed

to the physical loss of the catalyst during work-up over its repeated use (Figure **4.2**).

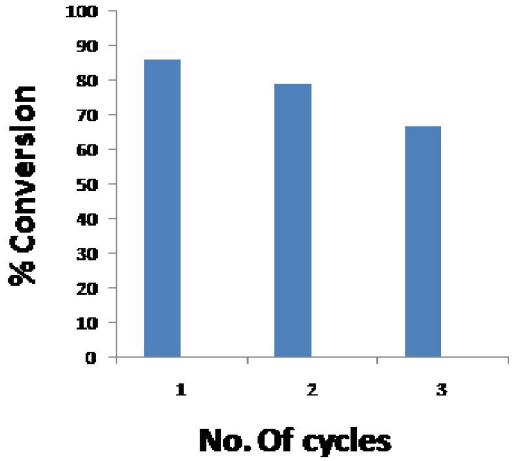


Figure **4.2** Recyclability of the catalyst

4.4.5 Characterisation of recycled catalyst

4.4.5.1 Powder X-Ray Diffraction (p-XRD) analysis: After successful completion of the C–S bond formation of heterocyclic thiols, the reaction mixture was treated with water and EtOAc. CuO NPs were recovered and collected from the aqueous solution by centrifugation. In addition, p-XRD analyses were done for both the fresh and recovered CuO NPs (after third cycle). Considering the spectrum of recovered catalyst, apart from the peaks of CuO NPs, additional peaks have also been observed (Figure **4.3**). This may be due to impurity or the substrates getting adsorbed on catalyst surface thereby blocking the active sites in the catalyst. Another possible reason could be the change in catalyst shape and structure when exposed to stimuli (such as heat, light and pressure) may result in decrease in catalyst efficiency. These are the possible reasons behind lower yield of the product obtained after third catalytic cycle (results and discussion, section **4.4.4**).

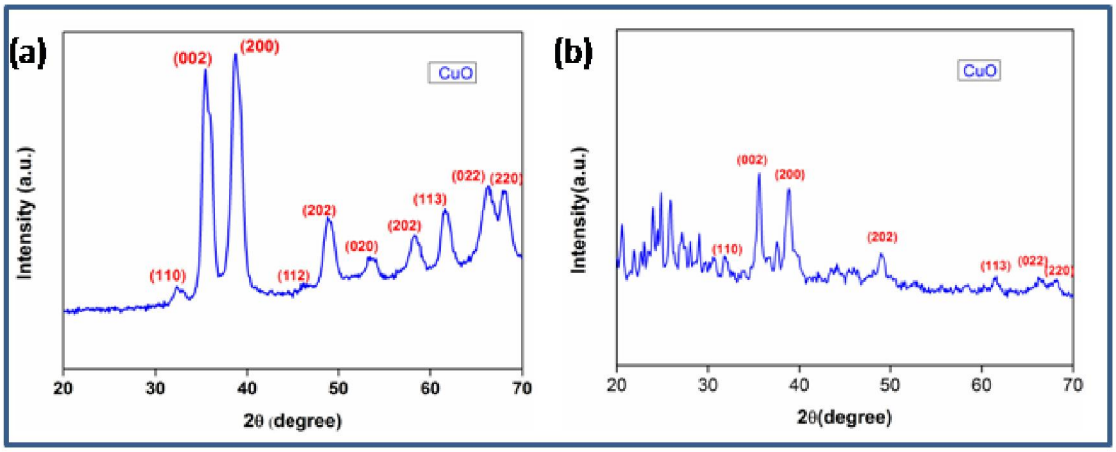


Figure **4.3** Powder X-ray diffraction patterns of (a) Fresh CuO NPs and (b) CuO NPs after the third catalytic cycle

4.4.5.2 Transmission Electron Microscopy (TEM) analysis: The TEM analysis of CuO NPs was compared before and after the reaction (third cycle). The experimental analysis showed identical particle shape and size in both the cases which clearly demonstrates that the reaction has taken a heterogeneous pathway and that the catalysis may occur on the surface of the CuO NPs (Figure **4.4**).

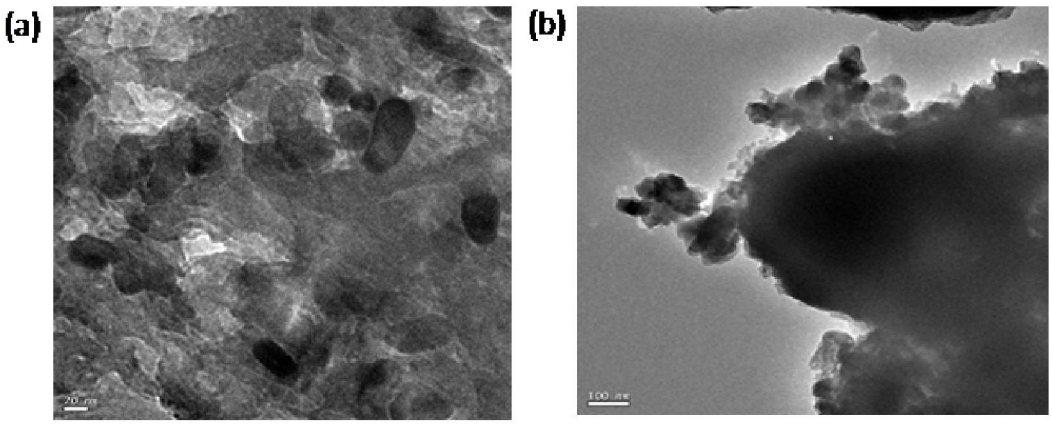
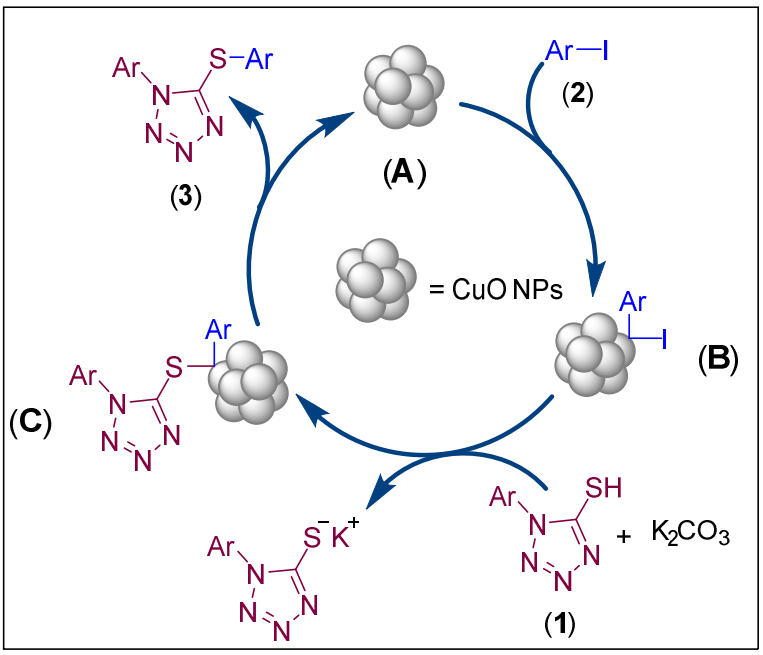


Figure **4.4** TEM images of (a) Fresh CuO NPs and (b) CuO NPs after the third catalytic cycle.

4.4.6 Mechanism

Based on literature findings and experimental analysis a plausible mechanism has been proposed for the reaction as shown in (Scheme **4.13**). Aryl halide (**2**) undergoes oxidative addition in presence of CuO NPs, **A** to give intermediate **B**. Further the nucleophile (**1**) undergoes reaction with the intermediate **B**, to give

intermediate **C.** The intermediate **C** then undergoes reductive elimination to deliver the final product **D** (**3**) and the cycle continues.



Scheme **4.13** Plausible mechanism for C-S cross-coupling reactions catalysed by CuO NPs

4.5 Conclusion

In this work, we explored a catalytic methodology for the direct *S*-2 arylation of varied heterocyclic thiols with aryl iodide derivatives using a relatively cheap and easily accessible form of copper. The developed protocol clearly demonstrated remarkable tolerance of the catalyst towards various functional groups. This protocol offers significant advantages in achieving C-S arylation without the use of any ligands. The true heterogeneity of the catalyst was demonstrated clearly with the retention of catalytic efficiency up to third cycles.

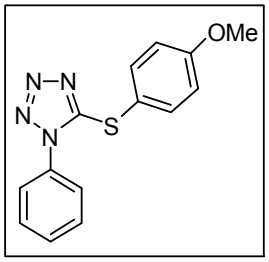
4.6 Experimental Section

4.6.1 General Experimental Procedure

CuO NPs (10 mol%) was added to a mixture of thiotetrazole (**1**, 0.5 mmol) and aryl iodides (**2**, 0.65 mmol) in DMF (3 mL) and the mixture was stirred at 100 °C for 5 hours. The progress of the reaction was monitored by TLC. On completion of the reaction, the crude mixture was extracted using ethyl acetate and washed with ice

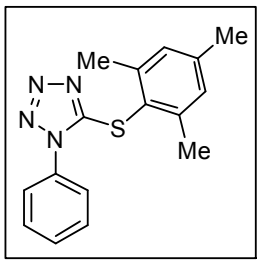
water. The organic layer was further concentrated under reduced pressure to obtain the crude product. The crude product was purified by column chromatography on silica gel (hexane–EtOAc, 90:10) to afford the *N*–arylated tetrazoles, **3**.

4.6.2 Characterisation data of the products



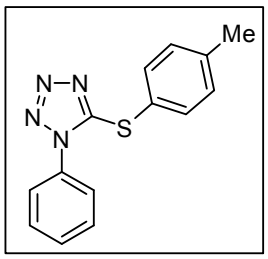
5-((4-methoxyphenyl)thio)-1-phenyl-1H-tetrazole (**3a**)

White solid (122.3 mg, 86%); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.56 (s, 5H), 7.50 (d, J = 8.8 Hz, 2H), 6.91 (d, J = 8.8 Hz, 2H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 136.5, 133.8, 130.3, 129.8, 124.4, 116.4, 115.4.



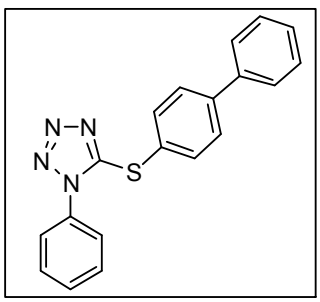
5-(mesitylthio)-1-phenyl-1H-tetrazole (**3b**)

White solid (118.56 gm, 80%); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.69–7.54 (m, 5H), 7.02 (s, 2H), 2.40 (s, 6H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 153.9, 143.3, 141.1, 133.9, 130.2, 129.9, 124.1, 21.8, 21.2.



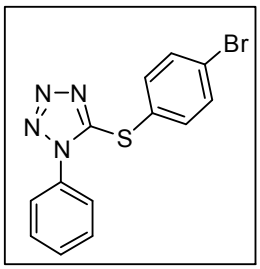
1-phenyl-5-(p-tolylthio)-1H-tetrazole (**3c**)

Colourless liquid (118 mg, 88%); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.55 (s, 7H), 7.45 (d, J = 8.2 Hz, 3H), 7.19 (d, J = 8.1 Hz, 3H), 2.35 (s, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.2, 140.7, 134.3, 133.7, 130.6, 130.4, 129.8, 124.4, 123.0, 21.3.



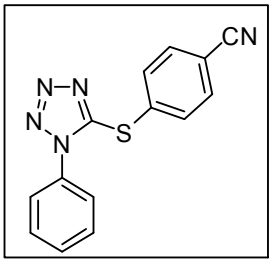
5-([1,1'-biphenyl]-4-ylthio)-1-phenyl-1H-tetrazole (**3d**)

Yellow solid (115.64 gm, 70%); ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 7.68–7.58 (m, 11H), 7.48 (t, J = 7.7 Hz, 2H), 7.44–7.39 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 153.7, 143.2, 139.8, 134.4, 133.7, 130.4, 129.8, 129.0, 128.5, 128.1, 127.2, 125.4, 124.5.



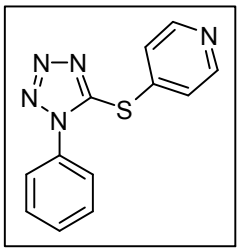
5-((4-bromophenyl)thio)-1-phenyl-1H-tetrazole (**3e**)

White solid (123.29 gm, 74%); ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 7.60 (p, J = 3.0, Hz, 3H), 7.59–7.53 (m, 4H), 7.49–7.44 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 153.1, 135.4, 133.5, 133.0, 130.5, 129.9, 125.8, 124.9, 124.4.



4-((1-phenyl-1H-tetrazol-5-yl)thio)benzonitrile (**3f**)

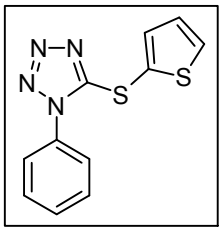
Off white (118.71 gm, 85%); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.84–8.57 (m, 2H), 7.99 (dd, J = 5.6, 3.9 Hz, 1H), 7.77–7.43 (m, 5H), 7.37 (dd, J = 7.9, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 153.6, 152.7, 151.0, 141.9, 133.3, 130.7, 130.0, 124.5.



4-((1-phenyl-1H-tetrazol-5-yl)thio)pyridine (**3g**)

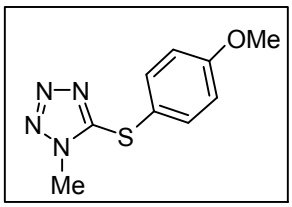
Colourless liquid (88 mg, 69%); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.71–7.62 (m, 1H), 7.62–7.50 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 151.6, 133.8, 133.1, 130.8, 130.0, 124.5, 117.8, 113.2.

1-phenyl-5-(thiophen-2-ylthio)-1H-tetrazole (**3h**)

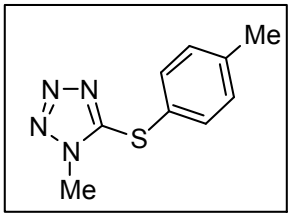


Yellow solid (87.21 gm, 67%); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.72–7.52 (m, 6H), 7.44 (dd, J = 5.1, 3.0 Hz, 1H), 7.22 (dd, J = 5.0, 1.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 153.4, 133.6, 131.6, 131.3, 130.4, 129.8, 127.3, 124.4, 120.5.

1-methyl-5-(p-tolylthio)-1H-tetrazole (**3i**)

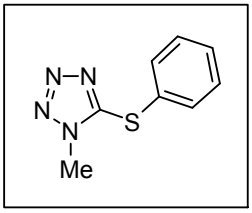


Brown solid (96.69 gm, 87%); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.63–7.45 (m, 2H), 7.03–6.88 (m, 2H), 3.96 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 161.1, 153.6, 135.6, 117.1, 115.6, 55.5, 33.9.



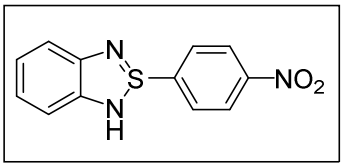
1-methyl-5-(p-tolylthio)-1H-tetrazole (**3j**)

Colourless solid (91.80 gm, 89%); ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 7.48–7.40 (m, 2H), 7.22 (d, J = 7.9 Hz, 2H), 3.96 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 152.9, 140.2, 133.0, 130.7, 123.8, 34.0, 21.2.



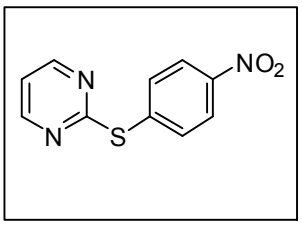
1-methyl-5-(phenylthio)-1H-tetrazole (**3k**)

Pale yellow liquid (192.24 mg, 82%); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.55–7.46 (m, 2H), 7.44–7.34 (m, 3H), 3.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 152.4, 132.4, 129.9, 129.5, 127.8, 34.1.



2-(4-nitrophenyl)-1H-2λ⁴-benzo[c][1,2,5]thiadiazole (**3l**)

Off white solid (88.2 mg, 65%); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.25 (d, J = 8.8 Hz, 2H), 7.97 (d, J = 8.1 Hz, 1H), 7.79 (d, J = 8.8 Hz, 3H), 7.56–7.43 (m, 1H), 7.39 (t, J = 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 162.8, 153.4, 147.9, 140.1, 132.7, 126.7, 125.6, 124.5, 122.8, 121.2.



2-((4-nitrophenyl)thio)pyrimidine (**3m**)

Pale yellow liquid (85 mg, 73%); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.47 (s, 2H), 7.68–7.57 (m, 2H), 7.48–7.37 (m, 3H), 6.94 (t, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.9, 157.6, 135.3, 129.8 – 129.2, 117.1.

4.6.3 Representative ^{1}H NMR and ^{13}C NMR spectra of a selected compound

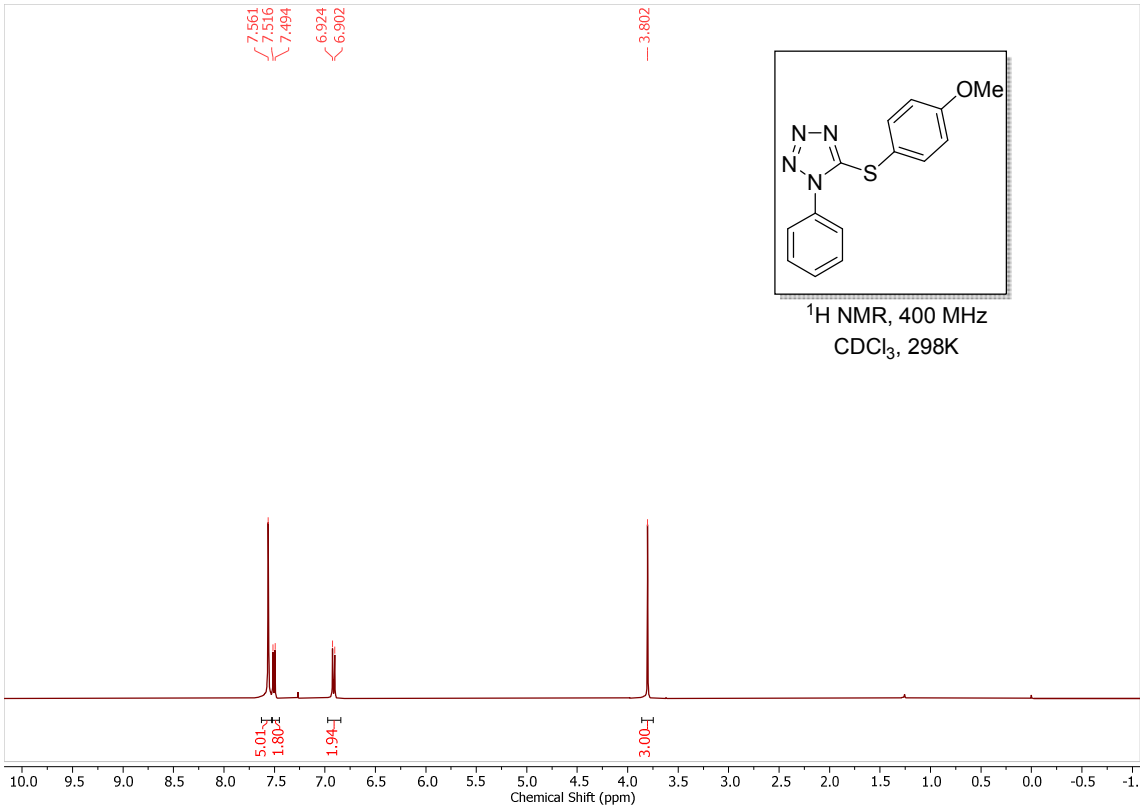


Figure **4.14** ^{1}H NMR Spectrum of **3a** in $CDCl_3$

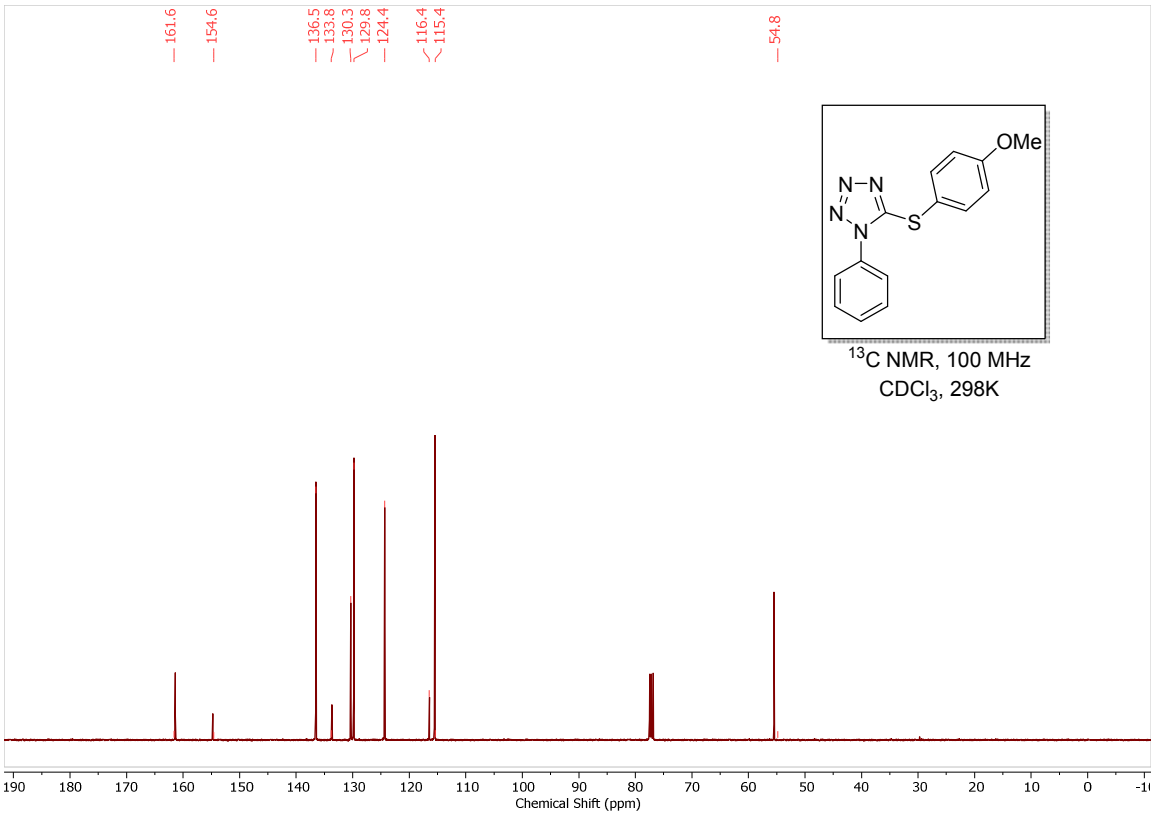


Figure **4.15** ^{13}C NMR Spectrum of **3a** in $CDCl_3$

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