The Journal of Organic Chemistry

Article

Synthesis of 1,2,4-Triazoles via Oxidative Heterocyclization: Selective C-N Bond Over C-S Bond Formation

Anupal Gogoi, Srimanta Guin, Suresh Rajamanickam, Saroj Kumar Rout, and Bhisma K. Patel

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.5b00956 • Publication Date (Web): 02 Sep 2015

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Synthesis of 1,2,4-Triazoles via Oxidative Heterocyclization: Selective C–N Bond Over C–S Bond Formation

Anupal Gogoi, Srimanta Guin, Suresh Rajamanickam,

Saroj Kumar Rout, and Bhisma K. Patel*

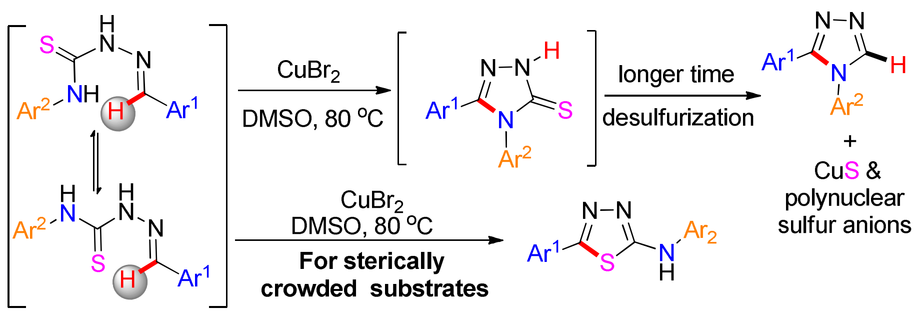
Department of Chemistry

Indian Institute of Technology Guwahati, Guwahati-781039, India

Fax: (+91)361-26909762.

E-mail: patel@iitg.ernet.in

RECEIVED DATE (will be automatically inserted after manuscript is accepted)



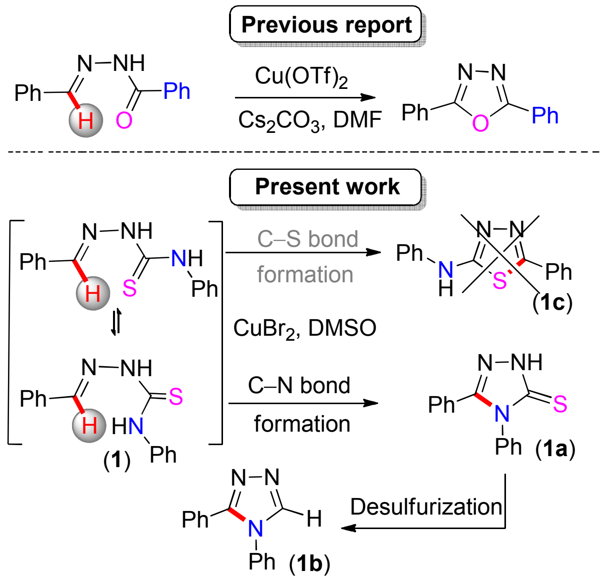
ABSTRACT: The higher propensity of C–N over C–S bond forming ability was demonstrated, through formal C–H functionalization during the construction of 4,5-disubstituted 1,2,4-triazole-3-thiones from arylidenearylthiosemicarbazides catalyzed by Cu(II). However, steric factor imparted by the *o*-disubstituted substrates tend to change the reaction path giving thiodiazole as the major or an exclusive product. Upon prolonging the reaction time, the *in situ* generated thiones are transformed to 4,5-disubstituted 1,2,4-triazoles via a desulfurization process. Two classes of heterocycles *viz.* 4,5-disubstituted 1,2,4-triazole-3-thiones and 4,5-disubstituted 1,2,4-triazoles can be synthesized from arylidenearylthiosemicarbazides by simply adjusting the reaction time. Desulfurization of 1,2,4-triazole-3-thiones is assisted by thiophilic Cu to provide 1,2,4-triazoles

with concomitant formation of CuS and polynuclear sulphur anions as confirmed from scanning electron microscope (SEM) and energy-dispersive X-ray spectroscopy (EDS) measurements. A one-pot synthesis of an anti-microbial compound has been successfully achieved following this strategy.

INTRODUCTION

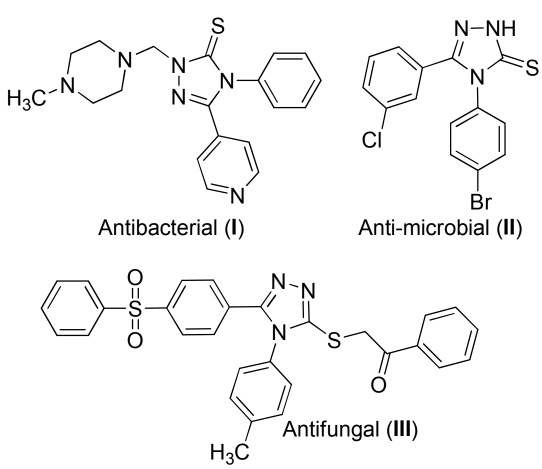
The non-requirement of substrate pre-functionalization leads to step and atom economy in transition metal catalyzed C–H bond functionalizations. Lately, the ubiquitous C–H bonds in organic compounds can be foreseen as quiescent synthetic equivalent of several useful functional groups. Because of the reduced number of steps in achieving the targeted synthesis these strategies are of paramount importance.[1] Of all C–H (sp, sp^2 and sp^3) bonds, the functionalizations of sp^2 C–H bonds of aromatics and hetero-aromatics have been well scrutinized.[2] However, analogous manipulation of imine sp^2 C–H bonds are relatively scarce. Some examples of late transition metal catalyzed imine C–H bond functionalizations are: (i) addition of 2-methylaza-arenes to imine catalyzed by Pd;[3a] (ii) benzonitrile addition to sulfenylamine catalyzed by Pd;[3b,c] (iii) oxidative coupling of arylimines with alkynes[3d] and 2-pyridyl[3e] using Rh and (iv) a Cu-catalyzed arylation of imine C–H bond in benzotriazepines.[3f] Besides, certain Cu-catalyzed heterocyclization reactions are known to proceed via oxidative C–O[3g] and/or C–N[3h,i] bond formations at imine C–H bonds. Some of the imine bonds containing substrates are reported to undergo skeletal rearrangements in the presence of transition metals.[4]

Scheme 1. Imine C–H bond Functionalization Leading to Heterocycles



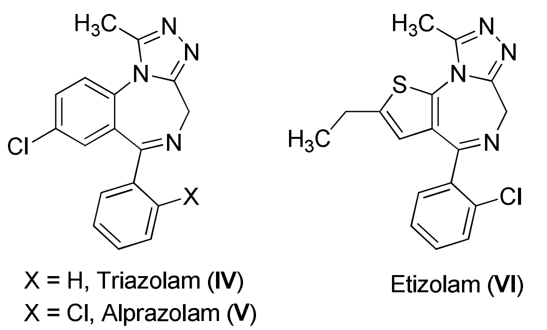
Recently we have achieved an elegant synthesis of 2,5-substituted 1,3,4-oxadiazole via C–H bond activation (C–O bond formation) involving an amidic carbonyl and an imine C–H bond in *N*-arylidenearoylhydrazide system.[3g] Herein, we wished to investigate if the imine C–H bond in arylidenearylthiosemicarbazide (**1**) can similarly be functionalized. If the C–H functionalization strategy works there exist two distinct possibilities *viz.* C–N bond or a C–S bond formation leading to the formation of either a *N*,5-diphenyl-1,3,4-thiadiazole-2-amine (**1c**) or a 4,5-diphenyl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (**1a**) as shown in Scheme 1.

Figure 1. Some Biologically Active 1,2,4-Triazole-3-thiones



Mercapto and thione derivatives of 1,2,4-triazoles are known to exhibit a variety of biological activities such as antibacterial,[7] antifungal,[8] antitumor,[9] anti-inflammatory,[10] antiviral,[11] antitubercular,[12] anticonvulsant[13] and antidepressant[14] activities. Some of the biologically active molecules bearing 1,2,4-triazole-3-thiones (**I**–**III**) as the core unit are shown in Figure 1. A myriad of applications of this scaffold has led to the development of various strategies for their synthesis. The common routes to 1,2,4-triazole-3-thiones include: (i) alkaline ring closure of acylthiosemicarbazides,[15] (ii) reaction of acid hydrazides with carbon disulfide and hydrazine hydrate,[16] (iii) cyclodehydration of *N*-(hydrazinecarbonothioyl)benzamides,[17] and (iv) thionation of 1,2,4-triazole-3-ones.[18]

Figure 2. Some Pharmaceuticals Possessing 1,2,4-Triazole Core



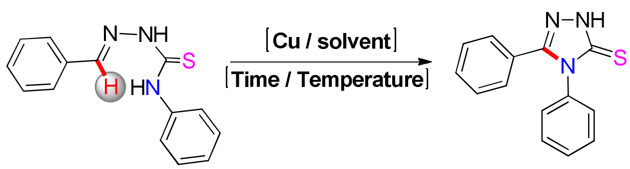
1,2,4-Triazoles and their derivatives are important class of heterocycles because of their prevalence in biologically active molecules including agrochemicals.[19-22] Pharmacological activities shown by derivatives of 1,2,4-triazoles include anti-inflammatory, CNS stimulants sedatives, antianxiety, antimicrobial agents, diuretic activities and antimycotic activities. Further, some of the drugs already available in market such as Triazolam (**IV**), Alprazolam (**V**) and Etizolam (**VI**) have 1,2,4-triazole ring system (Figure 2). Triazolam is used for treating insomnia under the brand name Halcion.[23a] Alprazolam (Xanax) is used to treat anxiety disorders, panic disorders, and anxiety caused by depression[23b] and Etizolam (Etizola) is used as an anxiolytic agent and hypnotic agent.[23c]

RESULTS AND DISCUSSION

With this objective and taking cues from our previous report[3g] arylidenearylthiosemicarbazide (**1**) was treated with 10 mol % of $Cu(OTf)_2$ in DMSO at 110 °C. The reaction after 2 h, provided a product in 23% yield. The structure was revealed to be 4,5-diphenyl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (**1a**) upon spectroscopic analysis. Thus, out of the two possibilities in Scheme 1, selective formation of C–N bond involving the thioamidic NH and an imine C–H bond is taking place. Similar oxidative C–N bond forming reactions have been reported recently both under metal[5] and metal free[6] conditions. Under the aforesaid reaction conditions there was substantial decomposition of starting material giving multitudes of unidentifiable side products; thus further optimization was necessary.

In pursuit to achieve an improved yield of thione (**1a**) from (**1**) various other reaction parameters such as catalyst quantity, salts of copper, solvents and reaction temperature were varied and the results are summarized in Table 1. Increasing the $Cu(OTf)_2$ loading to 20 mol % and 30 mol % resulted in an improved yield of the product (**1a**) (Table 1, entries 2-3). When the reaction was carried out at 80 °C instead of 110 °C, no significant difference in yield was observed (Table 1, entry 4). Among all other Cu(II)-salts [$Cu(ClO_4)_2.6H_2O$, $CuBr_2$, $CuSO_4.5H_2O$, $CuCl_2$, $Cu(OAc)_2$] and Cu(I) salts [CuCl and CuBr] tested, the use of $CuBr_2$ provided the best yield of (**1a**) (69%) in a shorter reaction time (Table 1, entries 5-11). Although catalysts $Cu(ClO_4)_2.6H_2O$ and $CuSO_4.5H_2O$ were equally effective in bringing about the transformation, but the time taken for completion of the reactions were longer compared to the use of $CuBr_2$. Except for DMSO, all other polar solvents like DMF, DMA, acetonitrile and non-polar solvent like 1,4-dioxane were unsuitable for this reaction (Table 1, entries 12-15). Addition of base to the reaction was not beneficial. When the reaction was carried out in the presence of a base Cs_2CO_3 (1 equiv) keeping all other parameters constant it gave poor yield of the desired product along with several other side products. No doubt at higher temperature (above 80 °C), triazole-thiones (Scheme 2) are formed rapidly but are also transform *in situ* to triazoles (Scheme 4). Thus higher temperature was not suitable for the formation of triazole-thiones (Scheme 2). Thus, the use of $CuBr_2$ (30 mol %) in DMSO solvent at 80 °C was found to be optimal, and substrate scope study was achieved using these conditions.

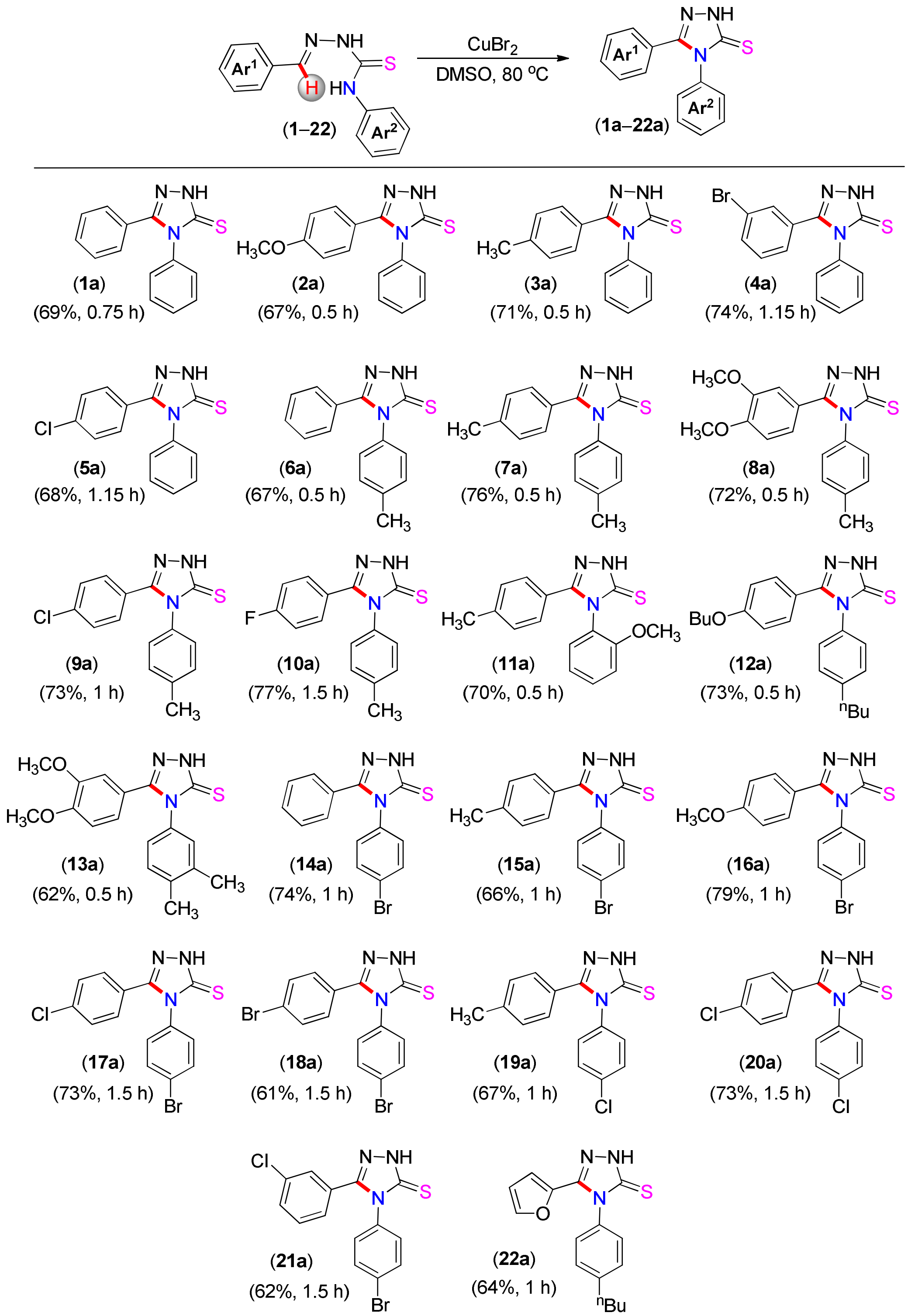
Table 1. Screening of Reaction Conditions



Entry	Catalyst (mol %)	Solvent	Temp(°C)	Time (h)	Yield[a] (%)
1	$Cu(OTf)_2$ (10)	DMSO	110	2	23
2	$Cu(OTf)_2$ (20)	DMSO	110	2	37
3	$Cu(OTf)_2$ (30)	DMSO	110	2	64
4	$Cu(OTf)_2$ (30)	DMSO	80	2	61
5	$Cu(ClO_4)_2.6H_2O$ (30)	DMSO	80	2	67
6	**$CuBr_2$ (30)**	**DMSO**	**80**	**0.75**	**69**
7	$CuSO_4.5H_2O$ (30)	DMSO	80	2	68
8	$CuCl_2$ (30)	DMSO	80	0.75	59
9	$Cu(OAc)_2$ (30)	DMSO	80	2	62
10	CuCl (30)	DMSO	80	2	60
11	CuBr (30)	DMSO	80	2	56
12	$CuBr_2$ (30)	DMF	80	0.75	0
13	$CuBr_2$ (30)	DMA	80	0.75	0
14	$CuBr_2$ (30)	Dioxane	80	0.75	0
15	$CuBr_2$ (30)	CH_3CN	80	0.75	15

[a]Isolated yield

Scheme 2. Substrate Scope for the Synthesis of of 1,2,4-Triazole-3-thiones from Arylidenearylthiosemicarbazides[a,b]

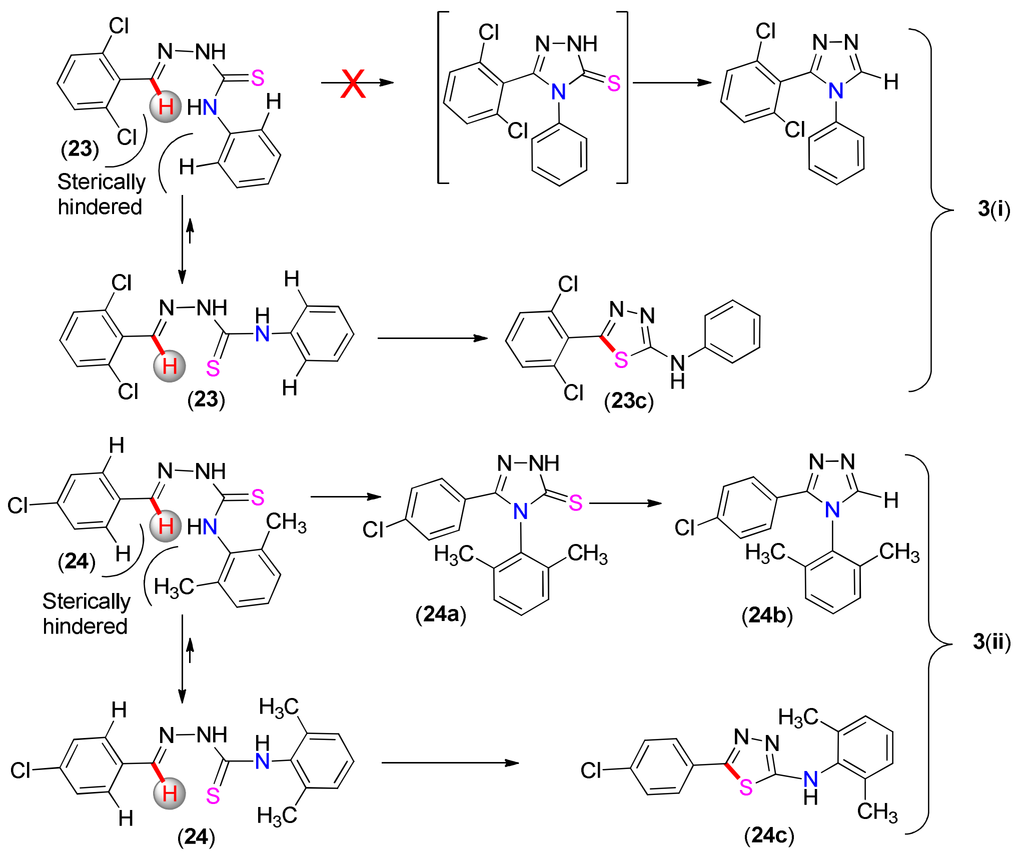


[a]Reaction conditions: *N*-arylidenearylthiosemicarbazide (0.5 mmol), $CuBr_2$ (0.15 mmol), in DMSO (2 mL) at 80 °C. [b]Isolated yields of pure product.

After figuring out the best optimum condition, we next explored the scope of various substrates leading to the formation of thiones. First, *N*-arylidenearylthiosemicarbazides derived from various substituted arylaldehydes were subjected to the present reaction conditions to see the effects of substitution. When the Ar^1 ring is substituted with electron-donating groups such as 4-OCH_3 (**2**), 4-CH_3 (**3**) or electron-withdrawing groups such as 3-Br (**4**), 4-Cl (**5**), all provided their corresponding 1,2,4-triazole-3-thiones (**2a**–**5a**) in yields ranging from 67-74%. No particular correlation between the electronic nature of the substituents and the yields of products could be ascertained; except slightly longer reaction times required for substrates (**4**) and (**5**) possessing electron-withdrawing groups (Scheme 2). When the aryl ring Ar^2 bears an electron-donating group such as 4-CH_3 and Ar^1 is unsubstituted as in (**6**), a moderate yield (67%) of the corresponding 1,2,4-triazole-3-thione (**6a**) was obtained. Various possible permutations and combinations of substituents in both the aryl (Ar^1 and Ar^2) rings of *N*-arylidenearylthiosemicarbazides were next investigated. Keeping the Ar^2 (4-CH_3) part constant, when the substituents in the Ar^1 ring were varied with either electron-donating [4-CH_3 (**7**) and 3,4-di-OCH_3 (**8**)] or electron-withdrawing [4-Cl (**9**) and 4-F (**10**)] groups all underwent effective cyclization via the formation of C–N bond. With other combinations of electron-donating substituents in the aryl rings [4-CH_3 and 2-OCH_3 (**11**), 4-OBu and 4-^{n}Bu (**12**), 3,4-di-OCH_3 and 3,4-di-CH_3 (**13**)], moderate to good yields of their respective thiones (**11a**–**13a**) were obtained in shorter reaction times. An electron-withdrawing group (4-Br) in Ar^2 and an unsubstituted Ar^1 ring as in (**14**), provided good yield (74%) of the thione (**14a**). Keeping the substituent 4-Br in ring Ar^2 and varying the substituents in ring Ar^1 *viz.* 4-CH_3 (**15**), 4-OCH_3 (**16**), 4-Cl (**17**) and 4-Br (**18**), desired thiones (**15a**–**18a**) were obtained in the range of 61-79% yields. Replacing 4-Br with 4-Cl in the Ar^2, and the Ar^1 having 4-CH_3 (**19**) and 4-Cl (**20**) substituents, a similar pattern in yields and reaction times were observed as with aforementioned 4-Br substituted (in Ar^2 ring) substrates (**15**–**18**). The structure of thione (**20a**) has been further confirmed by XRD analysis as shown in Figure S1 (see the Supporting Information).

The synthetic utility of this transformation has been demonstrated by the synthesis of an anti-microbial compound (**21a**)[7e] in 62% yield (Scheme 2) from its corresponding arylidenearylthiosemicarbazide (**21**). The reaction was also successful with *N*-arylidenethiosemicarbazide derived from a heterocyclic aldehyde, 2-furaldehyde (**22**), which gave a moderate yield (64%) of the corresponding thione (**22a**). Judging from the yield patterns in all the preceding set of substrates, it may be said that the electronic effects of substituents have no significant role in controlling the product yields.

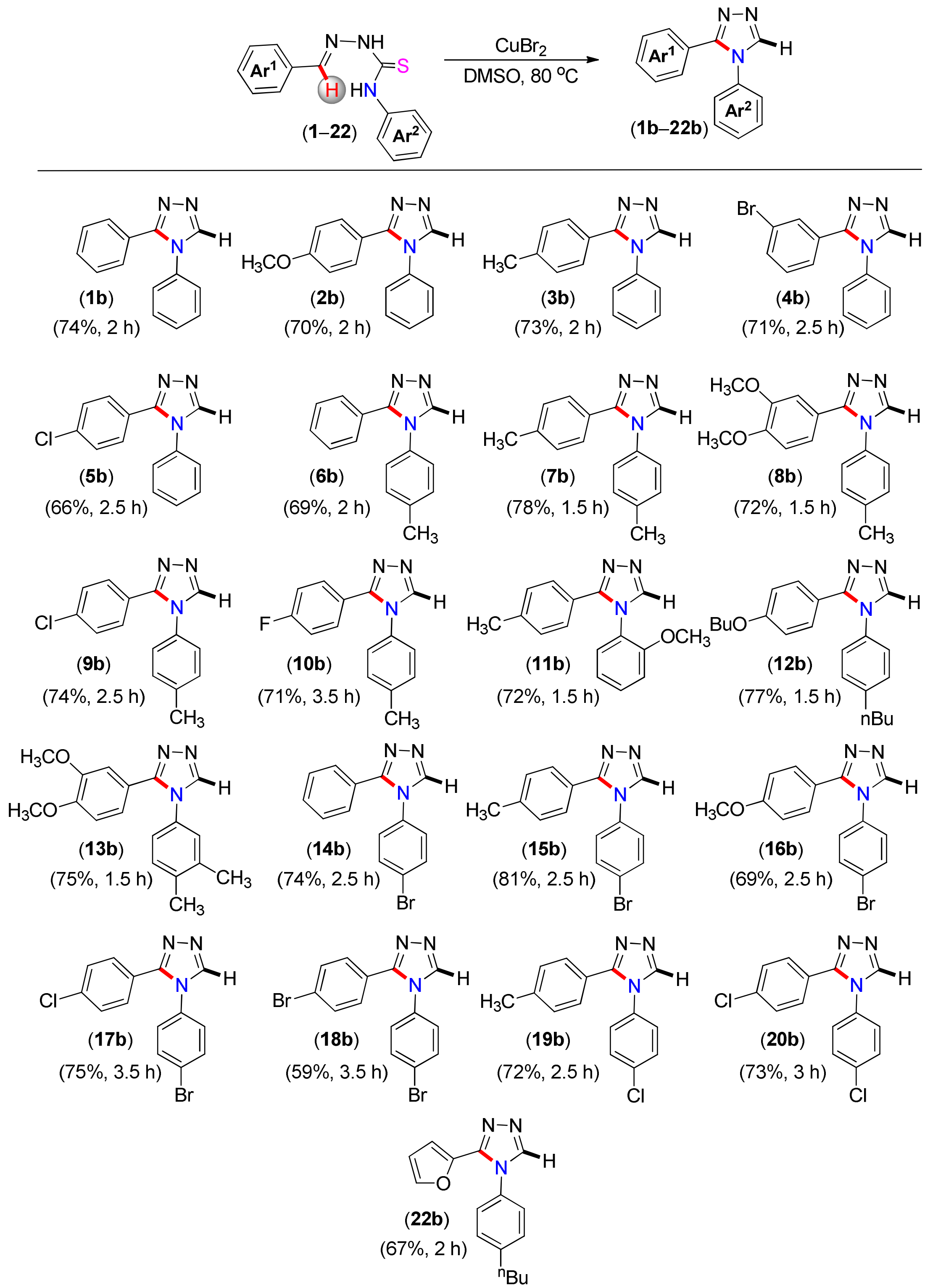
Scheme 3. Change in the Reactivity of Sterically Hindered Substrates



A complete change in the reactivity pattern was observed when any one of the aryl rings (derived from either aldehyde or thiosemicarbazide) in arylidenearylthiosemicarbazides is *ortho*-disubstituted. Arylidenearylthiosemicarbazides (**23**) derived from 2,6-dichlorobenzaldehyde gave exclusively 1,3,4-thiadiazole-2-amine (**23c**) and no traces of (**23a**) or (**23b**) (Scheme 3). Here, probably due to the extreme steric reason imparted by both *o*-chloro groups (Scheme 3(i)) the thiourea moiety in (**23**) adopted a *syn*-*syn* conformation as oppose to *syn*-*anti* conformation. This brings the sulphur atom to the proximity of imine C−H for oxidative cyclization (C−S bond formation) giving exclusively thiadiazole (**23c**). In yet another steric controlled reaction, arylidenearylthiosemicarbazide (**24**) derived from 2,6-dimethylthiosemicarbazide gave 1,3,4-thiadiazole-2-amine (**24c**) along with 1,2,4-triazole (**24b**) in the ratio of (3:2). Compound (**24b**) must have originated from its corresponding thione (**24a**) which however could not be isolated.

It may be mentioned here that during the optimization process, when the reaction (Table 1, entry 5) was prolonged, disappearance of the product (**1a**) and appearance of a new product having lower R_f than (**1a**) was observed. This product upon isolation and usual characterization by spectroscopic technique was found to be 1,2,4-triazole (**1b**) (Scheme 4) *i.e.* loss of a sulfur atom from the parent molecule. It is likely that the product (**1b**) might have formed via the desulfurization of (**1a**). To reconfirm the origin of the product (**1b**) when a preformed 4,5-diphenyl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (**1a**) was treated under the identical reaction conditions; 1,2,4-triazole (**1b**) was formed exclusively after 1.5 h, confirming our assumption. Thus, it was observed that by simply prolonging the reaction time, product (**1b**) was obtained exclusively. With progress in time the percentage formation of (**1a**) and (**1b**) varies. Percentage of (**1a**) and (**1b**) at different time (min) intervals are as follows: 30 min (55:00), 45 min (69:4), 60 min (58:15), 75 min (41:35), 90 min (20:57), 105 min (11:65) and 120 min (2:74).

Scheme 4. Substrate Scope for the Synthesis of 1,2,4-Triazoles from Arylidenearylthiosemicarbazides[a,b]

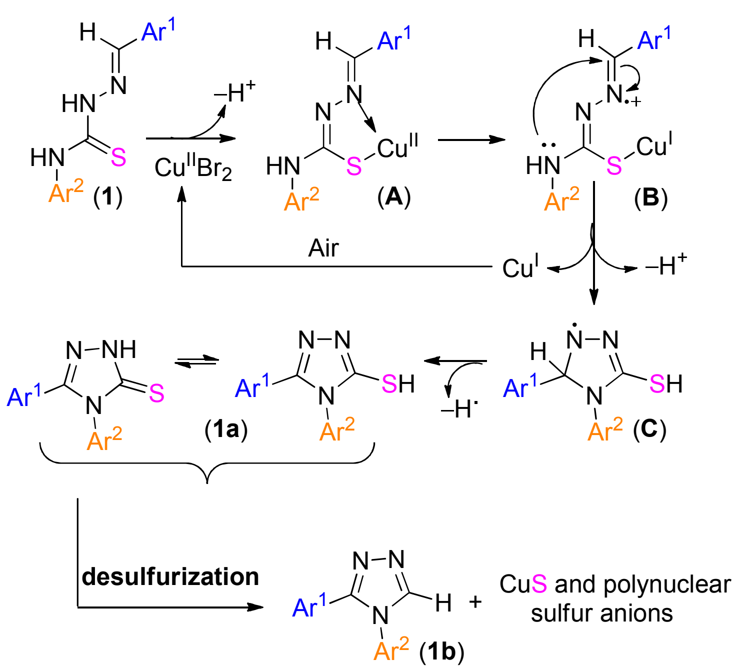


[a] Reaction conditions: *N*-arylidenearylthiosemicarbazide (0.5 mmol) , $CuBr_2$ (0.15 mmol), in DMSO (2 mL) at 80 °C. [b]Isolated yields of pure product.

The same thiosemicarbazides (**1**–**20**) and (**22**) which were used for the synthesis of thiones were now employed for the synthesis of a series of 4,5-diaryl-1,2,4-triazoles under the same reaction conditions but just by prolonging the reaction times. All the thiosemicarbazides underwent facile transformation to their respective triazoles (**1b**–**20b**) and (**22b**) via the loss of a sulphur atom from their intermediate thiones (Scheme 4). Structure of the compound (**7b**) has been unequivocally confirmed by X-ray crystallography as shown in Figure S2 (see the Supporting Information).

Here again, no correlation between electronic effects of substituents and yields of products were observed, but whatever little effect was seen it was similar to the one observed during the formaton of their thiones. However, the time taken for the completion of reaction was shorter for substrates possessing electron-donating groups on either one or both the aryl rings than for substrates bearing one or two electron-withdrawing groups. This observation is consistent with the formation of their intermediate thiones.

Scheme 5. Proposed Reaction Mechanism



A plausible mechanism for the formation of thione (**1a**) is proposed (Scheme 5) which is in accordance with the earlier reports on copper catalyzed oxidative heterocyclization.[3h,24] Copper(II) undergoes ligation with arylidenearylthiosemicarbazide (**1**) through its imine nitrogen and the soft sulfur atom to give a 5-membered complex (**A**). The co-ordinated Cu(II) is reduced to Cu(I) by a single electron transfer from the imine nitrogen resulting in the formation of a nitrogen centered radical cation (**B**). The Cu(I) generated in the medium is oxidized back to Cu(II) for the next catalytic cycle by the atmospheric oxygen. This type of reduction and reoxidation has been confirmed by EPR and UV-Vis spectroscopic studies by others.[24b] The formation of a radical cation (**B**) facilitates the nucleophilic attack onto its imine carbon by the terminal thioamidic nitrogen resulting in a nitrogen centred radical (**C**). Loss of a hydrogen radical from (**C**) gives the thione (**1a**). Similar cation radical and abstraction of H radical has been reported on analogous system using Cu(II).[25] It may be mentioned here that a $FeCl_3$ mediated cyclization of aldehydethiosemicarbazide (unsubstituted at N(2) nitrogen) gave 1,3,4-thiadiazolic product suggesting an intramolecular attack of *S*.[24c] However, for aldehydethiosemicarbazide substituted at N(2) nitrogen depending on the nature of substituents (EWG or EDG) either *S* or *N* intramolecular attack product is observed. For strongly electron withdrawing groups ($-NO_2$ and $-CF_3$) *S* attack product predominates over *N* attack product. No variation in *N* versus *S* attack product was observed for small change in the electronic effect. While a cupric perchlorate catalyzed cyclization of N(2) substituted aldehydethiosemicarbazide gave intramolecular *N*-attack product 1,2,4-triazole-3-thiones exclusively.[24c] This observation is consistent with our present cyclization involving aldehydethiosemicarbazide (unsubstituted at N(2) nitrogen). The exact pathway leading to the loss of sulphur to give 1,2,4-triazole (**1b**) is not clear at this moment. However, a similar desulfurization of (**1a**) under an oxidative condition *i.e.* in the presence of AcOH / hydrogen peroxide is reported.[26] To find out the origin of C-5 hydrogen in (**1b**), the reaction of substrate (**1**) was carried out in DMSO-d_6 under otherwise identical conditions, no deuterium incorporated product (***d*-1b**) was observed (Scheme 6 (i)). However, a deuterium incorporated product (***d*-1b**) along with a non deuterated product (**1b**) (Scheme 6 (ii)) were obtained in the ratio of 4:1 when the reaction was performed in the presence of DMSO : D_2O (1:1, 1 mL). When the isolated product (**1b**) was subjected to the present reaction condition, but in the presence of D_2O, a deuterium exchanged product (***d*-1b**) at C5-H was observed (Scheme 6, path-a). Thus the C-5 hydrogen is not originating from the solvent (DMSO) rather one of the proton (or deuterium, obtained by exchange of NH with D_2O) from nitrogen atom is transferred to C-5 position. Further the deuterated product (***d*-1b**) can be obtained from the non deuterated product (**1b**) in the presence of $CuBr_2$ and D_2O.

Scheme 6. Origin of C-5 Hydrogen

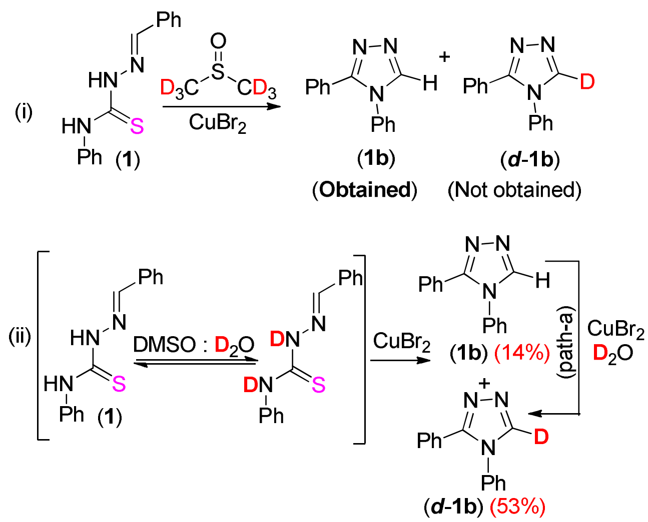
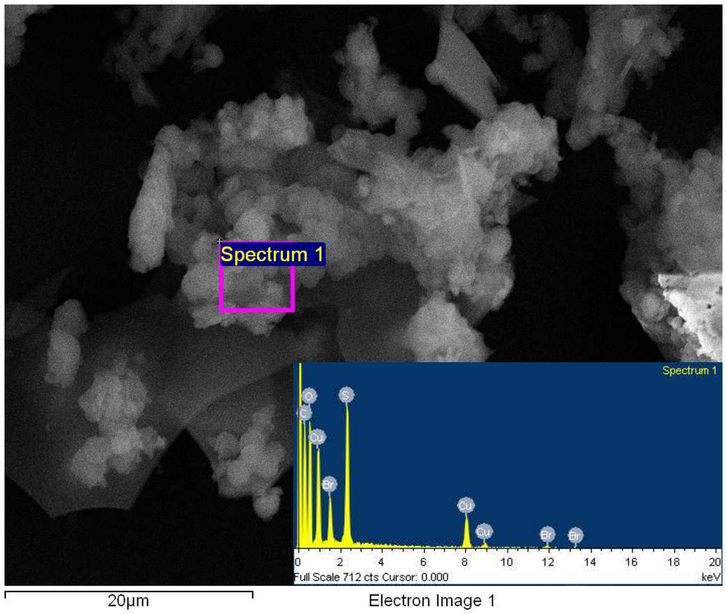


Figure 3. SEM and EDS Analysis of the Isolated Cu Salt.



Formation of CuS in the reaction medium has been confirmed by solid state UV (see the Supporting Information Figure S3).[27] If sulphur extrusion is by the formation of CuS alone, than a minimum of one equivalent of Cu salt is needed for the transformation of (**1a**) to (**1b**) (Scheme 5), however, a complete transformation is taking place with just 30 mol % of the $CuBr_2$. In addition to the formation of CuS a range of polynuclear anions containing sulphur rings or chains are possible and such has been observed by us earlier and also reported in literature.[28] As can be seen from SEM the flake like structures (Figure 3) resembles the formation of CuS/polysulfide which is also evident from the elemental composition from EDS analysis.

In conclusion, we developed an efficient Cu(II) catalyzed strategy for the synthesis of two important class of heterocycles *viz*. 4,5-disubstituted 1,2,4-triazole-3-thiones and 4,5-disubstituted 1,2,4-triazoles from arylidenearylthiosemicarbazides by simple tuning the reaction time. Oxidative C–N bond over C–S formations afforded 4,5-disubstituted 1,2,4-triazole-3-thiones and their desulfurization give 4,5-disubstituted 1,2,4-triazoles. However, steric factor imparted due to the presence of *o*-disubstituted substrates in any of the aryl rings of arylidenearylthiosemicarbazides, the reactivity pattern changes giving thiodiazole as the major or an exclusive product. The thiophilic Cu assist the desulfurization of thiones with concomitant formation of CuS or an array of polynuclear sulfur anions which has been analyzed and confirmed by SEM and EDS analysis. The synthetic utility of this strategy has been successfully applied for the synthesis of an anti-microbial compound (**21a**).

EXPERIMENTAL SECTION

General information:

All the compounds were commercial grade and were used without further purification. Organic extracts were dried over anhydrous sodium sulphate. Solvents were removed in a rotary evaporator under reduced pressure. Silica gel (60–120 mesh size) was used for the column chromatography. Reactions were monitored by TLC on silica gel 60 F254 (0.25 mm). NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 with tetramethylsilane as the internal standard for proton NMR (600 MHz) $CDCl_3$ and DMSO-d_6 solvent as internal standard for ^{13}C NMR (150 MHz). HRMS spectra were recorded using ESI mode (Q-TOF type Mass Analyzer). IR spectra were recorded in KBr or neat.

Crystallographic Description:

Crystal data were collected - using graphite monochromated MoKα radiation (λ = 0.71073 Å) at 298 K. Cell parameters were retrieved using SMART[31a] software and refined with SAINT[31a] on all observed reflections. Data reduction was performed with the SAINT software and corrected for Lorentz and polarization effects. Absorption corrections were applied with the program SADABS[31b]. The structure was solved by direct methods implemented in SHELX-97[31c] program and refined by full-matrix least-squares methods on F2. All non-hydrogen atomic positions were located in difference Fourier maps and refined anisotropically. The hydrogen atoms were placed in their geometrically generated positions. Colourless crystals were isolated in rectangular shape from methanol at room temperature.

*General Procedure for the Synthesis of (E)-2-Benzylidene-N-phenylhydrazinecarbothioamide (**1**):*

This compound can be prepared following the procedure as reported.[24c-d] However, we have adopted the following modified procedure.

To a solution of of *N*-phenylhydrazinecarbothioamide (334.4 mg, 2 mmol) in EtOH (5 mL) was added benzaldehyde (233.4, 2.2 mmol). The mixture was stirred under reflux for 1 h. The reaction mixture was then cooled to room temperature and the precipitate solid so obtained was filtered and washed with hexane (3 x 3 mL) to give (*E*)-2-benzylidene-*N*-phenylhydrazinecarbothioamide (**1**) (464.6 mg, 91%).

(E)-2-(4-Methylbenzylidene)-N-(p-tolyl)hydrazinecarbothioamide (7). White solid; yield 498.8 mg, 88%; mp 194–196 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.37 (s, 3H), 2.38 (s, 3H), 7.21 (t, *J* = 7.2 Hz, 4H), 7.49 (d, *J* = 7.8 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.96 (s, 1H), 9.12 (s, 1H), 10.57 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.3, 21.7, 125.2, 127.6, 129.6, 129.8, 130.6, 135.4, 136.4, 141.3, 143.5, 176.1; IR (KBr): 3303, 3145, 2986, 1593, 1549, 1515, 1498, 1408, 1308, 1262, 1210, 1191, 1071, 814, 734 cm^{-1}.

*(E)-2-(3,4-Dimethoxybenzylidene)-N-(p-tolyl)hydrazinecarbothioamide (**8**).* White solid; yield 553.4 mg, 84%; mp 185–187 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.37 (s, 3H), 3.92 (s, 3H), 3.93 (s, 3H), 6.88 (d, *J* = 8.4 Hz, 1H), 7.17 (d, *J* = 8.4 Hz, 1H), 7.21–7.23 (m, 3H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.90 (s, 1H), 9.05 (s, 1H), 10.27 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.3, 56.2, 56.3, 108.8, 111.1, 122.6, 125.4, 126.2, 129.7, 135.5, 136.5, 143.6, 149.6, 151.7, 176.1; IR (KBr): 3330, 3144, 2987, 2959, 1601, 1545, 1509, 1463, 1421, 1265, 1236, 1207, 1196, 1137, 1018, 801, 732 cm$^{-1.}$

*(E)-2-(4-Butoxybenzylidene)-N-(4-butylphenyl)hydrazinecarbothioamide (**12**).* White solid; yield 690.3 mg, 90%; mp 148–150 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.94 (t, *J* = 7.2 Hz, 3H), 0.99 (t, *J* = 7.2 Hz, 3H), 1.38 (sextet, *J* = 7.8 Hz, 2H), 1.50 (sextet, *J* = 7.2 Hz, 2H), 1.62 (quintet, *J* = 7.8

Hz, 2H), 1.78 (quintet, *J* = 7.2 Hz, 2H), 2.63 (t, *J* = 7.2 Hz, 2H), 3.99 (t, *J* = 6.6 Hz, 2H), 6.90 (d, *J* = 9.0 Hz, 2H), 7.22 (d, *J* = 7.8 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H) 7.59 (d, *J* = 9.0 Hz, 2H), 7.95 (s, 1H), 9.13 (s, 1H), 10.56 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 14.0, 14.1, 19.4, 22.5, 31.4, 33.7, 35.4, 68.0, 115.0, 124.9, 125.7, 128.9, 129.2, 135.6, 141.2, 143.4, 161.4, 175.6; IR (KBr): 3294, 3155, 2954, 2928, 1601, 1552, 1512, 1501, 1465, 1415, 1303, 1260, 1193, 1168, 1067, 1022, 971, 829 cm^{-1}.

*(E)-N-(4-Bromophenyl)-2-(4-methylbenzylidene)hydrazinecarbothioamide (**15**).* White solid; yield 585.3 mg, 86%; mp. 201–203 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.39 (s, 3H), 7.22 (d, *J* = 7.2 Hz, 2H), 7.51(d, *J* = 7.8 Hz, 2H), 7.57 (d, *J* = 7.2 Hz, 4H), 7.94 (s, 1H), 9.16 (s, 1H), 10.32 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.8, 119.5, 126.3, 127.7, 129.9, 130.3, 132.0, 137.1, 141.6, 144.0, 175.7; IR (KBr): 3315, 3145, 2989, 1604, 1586, 1547, 1502, 1400, 1329, 1262, 1199, 1067, 1009, 952, 931, 827, 810, 753 cm^{-1}.

*(E)-N-(4-Bromophenyl)-2-(4-methoxybenzylidene)hydrazinecarbothioamide (**16**).* White solid; ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.86 (s, 3H), 6.94 (d, *J* = 9.0 Hz, 2H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.87 (s, 1H), 9.13 (s, 1H), 9.89 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 55.7, 114.7, 119.4, 125.6, 126.2, 129.4, 132.0, 137.2, 143.5, 162.1, 175.6; IR (KBr): 3329, 3314, 3140, 2979, 1601, 1586, 1547, 1511, 1502, 1397, 1276, 1255, 1206, 1166, 1068, 1028, 1010, 826, 783 cm^{-1}.

*General Procedure for the Synthesis of 4,5-Diphenyl-2,4-dihydro-3H-1,2,4-triazole-3-thione (**1a**).*

To a solution of 1-benzylidene-4-phenylthiosemicarbazide (**1**) (127.67 mg, 0.5 mmol) in DMSO (2 mL) was added $CuBr_2$ (33.50 mg, 0.15 mmol) and the resultant solution was put into a preheated oil bath (80 ^{o}C) for 0.75 h. The reaction mixture was cooled to room temperature and admixed with water (5 mL) and the product was extracted with ethyl acetate (2 x 20 mL). The organic phase was dried over anhydrous sodium sulphate, filtered and concentrated in vacuo. The crude product was purified over a column of silica gel and eluted with (8:2 hexane / ethyl acetate) to give 4,5-diphenyl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (**1a**) (87.40 mg, 69 % yield).

Deuterium Exchange Experiment.

2-Benzylidene-*N*-phenylhydrazinecarbothioamide (**1**) (63.84 mg, 0.25 mmol) was taken in a 10 mL round bottom flask. To which was added DMSO (0.5 mL) and D_2O (0.5 mL) and the mixture was stirred at room temperature for 3 h. Then $CuBr_2$ (16.75 mg, 0.075 mmol) was added to it and the resultant reaction mixture was put into a preheated oil bath (80 ^{o}C) for 2 h. After completion of the reaction it was admixed with water (5 mL) and the product was extracted with ethyl acetate (2 x 20 mL). The organic phase was dried over anhydrous sodium sulphate and concentrated in vacuo. The crude product was purified over a column of silica gel and eluted with (8:2 hexane / ethyl acetate) to give deuterated product (***d*-1b**) and non-deuterated product (**1b**). The ratio of deuterated product (***d*-1b**) and non-deuterated product (**1b**) was determined by ^{1}H NMR. The ratio of (***d*-1b**) : (**1b**) was found to be 4:1 (See Supporting Information).

*4,5-Diphenyl-2,4-dihydro-3H-1,2,4-triazole-3-thione (**1a**).* White solid; yield 87 mg, 69%; mp 275–278 ^{o}C (Lit[29a] mp 291–292 ^{o}C, Yield 93%); ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.30–7.36 (m, 6H), 7.40 (t, J = 7.8 Hz, 1H), 7.48–7.49 (m, 3H), 14.14 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 125.8, 128.2, 128.5, 128.7, 129.3, 129.4, 130.3, 134.5, 150.5, 168.6; IR (KBr): 3436, 3103, 2927, 2746, 1546, 1506, 1445, 1402, 1335, 1275, 1243, 1077, 969, 770, 701, 690, 609 cm^{-1}; HRMS (ESI): calcd. for $C_{14}H_{12}N_3S^+$ [M + H$^+$] 254.0746; found 254.0753.

*5-(4-Methoxyphenyl)-4-phenyl-2,4-dihydro-3H-1,2,4-triazole-3-thione (**2a**).*[29b] White solid; yield 95 mg, 67%; mp 270–272 ^{o}C; ^{1}H NMR (600 MHz, DMSO-d_6): δ 3.72 (s, 3H), 6.88 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 9.0 Hz, 2H), 7.33–7.34 (m, 2H), 7.48-7.50 (m, 3H), 14.03 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 55.3, 114.0, 117.9, 128.7, 129.3, 129.4, 129.7, 134.7, 150.4, 160.6, 168.4; IR (KBr): 3434, 3093, 2929, 1612, 1516, 1426, 1391, 1330, 1255, 1179, 1025, 968, 838, 752, 694, 594 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{14}N_3OS^+$ [M + H$^+$] 284.0852; found 284.0857.

*5-(4-Methylphenyl)-4-phenyl-2,4-dihydro-3H-1,2,4-triazole-3-thione (**3a**).*[29c] White solid; yield 95 mg, 71%; mp 261–263 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.32 (s, 3H), 7.08 (d, J = 7.8 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 7.31–7.32 (m, 2H), 7.49–7.51 (m, 3H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 20.8, 122.9, 128.1, 128.7, 129.1, 129.3, 129.4, 134.6, 140.2, 150.6, 168.5; IR (KBr): 3081, 3010, 2921, 1514, 1497, 1420, 1329, 1278, 1240, 970, 822, 725, 696, 589 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{14}N_3S^+$ [M + H$^+$] 268.0903; found 268.0915.

*5-(3-Bromophenyl)-4-phenyl-2,4-dihydro-3H-1,2,4-triazole-3-thione (**4a**).* Light yellow solid; yield 123 mg, 74%; mp 223–225 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.28–7.31 (m, 2H), 7.37–7.39 (m, 2H), 7.45 (s, 1H), 7.50–7.53 (m, 3H), 7.60–7.62 (m, 1H), 14.21 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 121.5, 127.2, 127.9, 128.7, 129.4, 129.5, 130.6, 130.8, 133.1, 134.3, 149.1, 168.7; IR (KBr): 3436, 3080, 2921, 1542, 1490, 1475, 1402, 1331, 1302, 1280, 1240, 975, 801, 715, 698, 618 cm^{-1}; HRMS (ESI): calcd. for $C_{14}H_{11}{}^{79}BrN_3S^+$ [M + H$^+$] 331.9852; found 331.9844.

*5-(4-Chlorophenyl)-4-phenyl-2,4-dihydro-3H-1,2,4-triazole-3-thione (**5a**).* White solid; yield 98 mg, 68%; mp 270–272 °C (Lit[15l] mp 271–272 °C, Yield 88%); ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.25 (d, J = 9.0 Hz, 2H), 7.28–7.30 (m, 2H), 7.32 (d, J = 8.4 Hz, 2H), 7.46-7.48 (m, 3H), 14.12 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6 + $CDCl_3$): δ 124.5, 128.5, 128.7, 129.4, 129.5, 129.8, 134.3, 135.5, 149.5, 168.8; IR (KBr): 3057, 2915, 1599, 1540, 1499, 1452, 1416, 1329, 1279, 1238, 1091, 1015, 970, 835, 744, 696 cm^{-1}; HRMS (ESI): calcd. for $C_{14}H_{11}{}^{35}ClN_3S^+$ [M + H$^+$] 288.0357; found 288.0353.

*4-(4-Methylphenyl)-5-phenyl-2,4-dihydro-3H-1,2,4-triazole-3-thione (**6a**).*[29a] White solid; yield 90 mg, 67%; mp 219–221 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.40 (s, 3H), 7.17 (d, J = 8.4 Hz, 2H), 7.27–7.28 (m, 4H), 7.32 (d, J = 7.2 Hz, 2H), 7.36 (t, J = 7.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.6, 125.7, 128.1, 128.4, 128.8, 130.6, 130.8, 131.9, 140.2, 151.6, 169.6; IR (KBr): 3109, 3033, 2933, 1548, 1516, 1500, 1482, 1445, 1398, 1333, 1276, 1239, 968, 819, 771, 696, 603 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{14}N_3S^+$ [M + H$^+$] 268.0903; found 268.0915.

*4,5-Bis(4-methylphenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione (**7a**)*. White solid; yield 107 mg, 76%; mp 233–235 °C (Lit[29d] mp 220–222 °C, Yield 78%); ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.30 (s, 3H), 2.40 (s, 3H), 7.07 (d, *J* = 7.8 Hz, 2H), 7.16 (d, *J* = 7.8 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 12.27 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.57, 21.59, 122.8, 128.2, 128.3, 129.6, 130.6, 132.1, 140.2, 141.2, 151.7, 169.6; IR (KBr): 3090, 2923, 1614, 1514, 1486, 1420, 1329, 1243, 1243, 1020, 969, 818, 717, 583 cm^{-1}; HRMS (ESI): calcd. for $C_{16}H_{16}N_3S^+$ [M + H^+] 282.1059; found 282.1055.

*5-(3,4-Dimethoxyphenyl)-4-(4-methylphenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione (**8a**)*.[29e] Brown solid; yield 118 mg, 72%; mp 215–217 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ 2.36 (s, 3H), 3.51 (s, 3H),3.72 (s, 3H), 6.82 (s, 1H), 6.86 (d, *J* = 7.8 Hz, 1H), 6.90–6.92 (m, 1H), 7.21 (d, *J* = 7.8 Hz, 2H), 7.31 (d, *J* = 7.8 Hz, 2H), 14.01 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 20.7, 55.1, 55.5, 111.35, 111.41, 117.9, 121.1, 128.5, 129.8, 132.3, 139.0, 148.2, 150.3, 150.4, 168.6; IR (KBr): 3273, 2929, 1608, 1515, 1477, 1464, 1397, 1335, 1286, 1257, 1234, 1137, 1018, 821, 769, 715, 583 cm^{-1}; HRMS (ESI): calcd. for $C_{17}H_{18}N_3O_2S^+$ [M + H^+] 328.1114; found 328.1107.

*5-(4-Chlorophenyl)-4-(4-methylphenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione (**9a**)*. White solid; yield 110 mg, 73%; mp 223–226 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ 2.33 (s, 3H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.27-7.31 (m, 4H), 7.42 (d, *J* = 8.4 Hz, 2H), 14.12 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 20.7, 124.7, 128.3, 128.7, 129.8, 130.0, 131.7, 135.2, 139.0, 149.7, 168.8; IR (KBr): 3062, 3033, 2903, 1544, 1513, 1472, 1428, 1416, 1375, 1328, 1234, 1091, 1039, 1016, 832, 818, 745, 615 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{13}{}^{35}ClN_3S^+$ [M + H^+] 302.0513; found 302.0516.

*5-(4-Fluorophenyl)-4-(4-methylphenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione (**10a**)*. White solid; yield 110 mg, 77%; mp 222–224 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.42 (s, 3H), 6.98 (t, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.33–7.35 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.6, 116.1 (d, *J* = 21.9 Hz), 121.9, 128.1, 130.6 (d, *J* = 8.7 Hz), 130.7, 131.7, 140.4, 150.7, 164.0 (d, *J* = 251.3 Hz), 169.4; IR (KBr): 3075, 2923, 1609, 1510, 1422, 1391, 1329, 1277, 1235, 1159, 971, 844, 816, 732, 718, 584 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{13}FN_3S^+$ [M + H$^+$] 286.0809; found 286.0817.

4-(2-Methoxyphenyl)-5-(4-methylphenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione ***(11a)***. White solid; yield 104 mg, 70%; mp 256–259 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.24 (s, 3H), 3.54 (s, 3H), 7.07 (t, J = 7.2 Hz, 1H), 7.11–7.13 (m, 3H), 7.18 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 7.8 Hz, 1H), 7.46 (t, J = 7.8 Hz, 1H), 14.01 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 20.8, 55.8, 112.9, 120.9, 123.1, 123.3, 127.2, 129.1, 130.4, 131.3, 140.2, 151.1, 154.5, 168.8; IR (KBr): 3436, 3082, 2924, 1603, 1509, 1464, 1430, 1326, 1259, 1183, 1118, 1022, 824, 757, 593 cm^{-1}; HRMS (ESI): calcd. for $C_{16}H_{16}N_3OS^+$ [M + H$^+$] 298.1009; found 298.1001.

4-(4-Butylphenyl)-5-(4-butoxyphenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione ***(12a)***. White solid; yield 139 mg, 73%; mp 200–202 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.95 (t, J = 7.2 Hz, 6H), 1.38 (q, J = 7.8 Hz, 2H), 1.45 (q, J = 7.2 Hz, 2H), 1.64 (quintet, J = 7.8 Hz, 2H), 1.73 (quintet, J = 7.2 Hz, 2H), 2.68 (t, J = 7.8 Hz, 2H), 3.92 (t, J = 6.6 Hz, 2H), 6.77 (d, J = 8.4 Hz, 2H), 7.20–7.24 (m, 4H), 7.29 (d, J = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 13.9, 14.1, 19.3, 22.5, 31.3, 33.3, 35.5, 67.9, 114.7, 117.7, 128.2, 129.8, 129.9, 132.2, 144.9, 151.5, 161.0, 168.9; IR (KBr): 3436, 3086, 2927, 2867, 1608, 1513, 1397, 1329, 1253, 1178, 1029, 968, 835, 738, 593 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{28}N_3OS^+$ [M + H$^+$] 382.1948; found 382.1942.

5-(3,4-Dimethoxyphenyl)-4-(3,4-dimethylphenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione ***(13a)***. Light brown solid; yield 106 mg, 62%; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.28 (s, 3H), 2.32 (s, 3H), 3.65 (s, 3H), 3.86 (s, 3H), 6.74 (d, J = 8.4 Hz, 1H), 6.90–6.92 (m, 2H), 7.07 (d, J = 8.4 Hz, 1H), 7.10 (s, 1H), 7.27–7.28 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 19.8, 20.0, 55.8, 56.1, 111.0, 118.1, 121.5, 125.8, 129.2, 131.0, 132.5, 138.7, 138.9, 148.9, 150.9, 151.3, 169.3; IR (KBr): 3442, 3081, 2923, 1607, 1516, 1460, 1399, 1342, 1258, 1229, 1142, 1023, 863, 823, 768, 716, 596 cm^{-1}; HRMS (ESI): calcd. for $C_{18}H_{20}N_3O_2S^+$ [M + H$^+$] 342.1271; found 342.1274.

4-(4-Bromophenyl)-5-phenyl-2,4-dihydro-3H-1,2,4-triazole-3-thione ***(14a)***.[29a] White solid; yield 123 mg, 74%; mp 204–206 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.32–7.38 (m, 6H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 2H), 14.17 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 122.6, 125.6, 128.4, 128.6, 130.4, 131.0, 132.3, 133.9, 150.4, 168.5; IR (KBr): 3078, 2925, 1616, 1547, 1491, 1396, 1329, 1278, 1235, 1021, 968, 825, 771, 695, 609 cm^{-1}; HRMS (ESI): calcd. for $C_{14}H_{11}{}^{79}BrN_3S^+$ [M + H$^+$] 331.9852; found 331.9857.

4-(4-Bromophenyl)-5-(4-methylphenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione ***(15a)***. White solid; yield 114 mg, 66%; mp 226–228 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ 2.26 (s, 3H), 7.16 -7.20 (m, 4H), 7.30 (d, *J* = 9.0 Hz, 2H), 7.68 (d, *J* = 9.0 Hz, 2H), 14.13 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 21.0, 122.79, 122.84, 128.4, 129.4, 131.1, 132.5, 134.0, 140.6, 150.7, 168.5; IR (KBr): 3060, 2919, 1546, 1513, 1492, 1418, 1393, 1330, 1281, 1238, 1070, 969, 821, 766, 716, 651, 588 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{13}{}^{79}BrN_3S^+$ [M + H$^+$] 346.0008; found 346.0019.

4-(4-Bromophenyl)-5-(4-methoxyphenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione ***(16a)***. White solid; yield 143 mg, 79%; mp 233–235 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ 3.73 (s, 3H), 6.92 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 7.8 Hz, 2H), 7.70 (d, *J* = 7.8 Hz, 2H), 14.10 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 55.3, 114.1, 117.7, 122.6, 129.9, 131.0, 132.3, 134.0, 150.3, 160.7, 168.2; IR (KBr): 3434, 3074, 2924, 1609, 1508, 1395, 1328, 1256, 1178, 1073, 1022, 968, 833, 591 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{13}{}^{79}BrN_3OS^+$ [M + H$^+$] 361.9957; found 361.9962.

4-(4-Bromophenyl)-5-(4-chlorophenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione ***(17a)***. White solid; yield 134 mg, 73%; mp 272–275 °C (Lit[29f] Yield 82%); ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.32–7.36 (m, 4H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 2H), 14.22 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 122.7, 124.5, 128.8, 130.2, 130.9, 132.4, 133.6, 135.3, 149.5, 168.5; IR (KBr): 3436, 3062, 2920, 1604, 1489, 1425, 1369, 1324, 1255, 1091, 1011, 830, 731, 614, 550 cm^{-1}; HRMS (ESI): calcd. for $C_{14}H_{10}{}^{79}Br^{35}ClN_3S^+$ [M + H$^+$] 365.9462; found 365.9450.

4,5-Bis(4-bromophenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione ***(18a)***. White solid; yield 125 mg, 61%; mp 266–269 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.26 (d, J = 7.8 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 7.60 (d, J = 8.4 Hz, 2H), 7.71 (d, J = 8.4 Hz, 2H), 14.21 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 122.7, 124.2, 124.9, 130.4, 130.9, 131.7, 132.4, 133.6, 149.6, 168.6; IR (KBr): 3437, 3061, 3024, 2922, 1597, 1543, 1492, 1413, 1328, 1232, 1069, 1024, 1010, 820, 735, 725, 613 cm^{-1}; HRMS (ESI): calcd. for $C_{14}H_{10}{}^{79}Br_2N_3S^+$ [M + H$^+$] 409.8957; found 409.8951.

4-(4-Chlorophenyl)-5-(4-methylphenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione ***(19a)***. White solid; yield 101 mg, 67%; mp 226–228 °C (Lit[29g] mp 144–146 °C, Yield 49%); ^{1}H NMR (600 MHz, CDCl$_3$): δ 2.34 (s, 3H), 7.12 (d, J = 7.8 Hz, 2H), 7.20 (d, J = 7.8 Hz, 2H), 7.27 (d, J = 9.0 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H); ^{13}C NMR (150 MHz, CDCl$_3$): δ 21.6, 122.4, 128.4, 129.7, 129.8, 130.2, 133.1, 136.1, 141.5, 151.5, 169.3; IR (KBr): 3440, 3084, 2923, 1513, 1497, 1384, 1330, 1094, 969, 821, 721, 590 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{13}{}^{35}ClN_3S^+$ [M + H$^+$] 302.0513; found 302.0502.

4,5-Bis(4-chlorophenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione ***(20a)***. Light brown solid; yield 118 mg, 73%; mp 223–226 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.29 (d, J = 8.4 Hz, 2H), 7.38-7.43 (m, 4H), 7.54 (d, J = 8.4 Hz, 2H), 14.12 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 124.5, 128.8, 129.4, 130.2, 130.6, 133.2, 134.1, 135.3, 149.6, 168.8; IR (KBr): 3437, 3064, 2919, 1604, 1496, 1414, 1326, 1276, 1238, 1094, 968, 837, 744 cm^{-1}; HRMS (ESI): calcd. for $C_{14}H_{10}{}^{35}Cl_2N_3S^+$ [M + H$^+$] 321.9967; found 321.9957. $C_{14}H_9Cl_2N_3S$, crystal dimensions 0.41 x 0.35 x 0.25mm, M_r = 322.20, Monoclinic, space group P21/c, a =6.2831(3), b = 11.0852(6), c = 21.1130(11) Å, α = 90 °, β = 92.069(3) °, γ = 90 °, V = 1469.55(13) Å^3, Z = 4, ρ_{calcd} = 1.456 g/cm^3, μ = 0.575 mm^{-1}, F(000) = 656.0, reflection collected / unique = 3689 / 2467, refinement method = full-matrix least-squares on F^2, final R indices [$I > 2\sigma(I)$]: R_1 = 0.0567, wR_2 = 0.1652, R indices (all data): R_1 = 0.0880, wR_2 = 0.1814, goodness of fit = 1.087. CCDC-1055788 for 3,4-Bis-(4-chlorophenyl)-4*H*-1,2,4-triazole (20*a*) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

*4-(4-Bromophenyl)-5-(3-chlorophenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione (**21a**)*. White solid; yield 114 mg, 62%; mp 228–230 °C (Lit[7e] mp 224–226 °C, Yield 95%); ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.23 (d, J = 7.8 Hz, 1H), 7.36–7.41 (m, 4H), 7.51 (d, J = 7.8 Hz, 1H), 7.72 (d, J = 8.4 Hz, 2H), 14.25 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 122.8, 127.1, 127.6, 128.2, 130.4, 130.6, 130.9, 132.4, 133.2, 133.6, 149.2, 168.6; IR (KBr): 3443, 3060, 2920, 1541, 1491, 1435, 1329, 1281, 1237, 1069, 980, 825, 783, 713, 614 cm^{-1}; HRMS (ESI): calcd. for $C_{14}H_{10}{}^{79}Br^{35}ClN_3S^+$ [M + H$^+$] 365.9462; found 365.9471.

*4-(4-Butylphenyl)-5-(furan-2-yl)-2,4-dihydro-3H-1,2,4-triazole-3-thione (**22a**)*. Brown solid; yield 96 mg, 64%; mp 202-205 °C; ^{1}H NMR (600 MHz, CDCl$_3$): δ 0.97 (t, J = 7.2 Hz, 3H), 1.38–1.44 (m, 2H), 1.68 (quintet, J = 7.8 Hz, 2H), 2.72 (t, J = 7.8 Hz, 2H), 5.90–5.91 (m, 1H), 6.32–6.33 (m, 1H), 7.26–7.27 (m, 2H), 7.37 (d, J = 7.8 Hz, 2H), 7.47 (s, 1H); ^{13}C NMR (150 MHz, CDCl$_3$): δ 14.1, 22.6, 33.4, 35.6, 111.6, 113.1, 128.1, 130.0, 131.5, 140.2, 144.3, 144.9, 145.8, 169.0; IR (KBr): 3437, 3084, 2925, 2863, 2774, 1621, 1523, 1452, 1325, 1280, 1247, 1024, 977, 839, 752, 624 cm^{-1}; HRMS (ESI): calcd. for $C_{16}H_{18}N_3OS^+$ [M + H$^+$] 300.1165; found 300.1161.

*3,4-Diphenyl-4H-1,2,4-triazole (**1b**)*. White solid; yield 82 mg, 74%; mp 147–149 °C (Lit[30a] mp 153–155 °C, Yield 95%); ^{1}H NMR (600 MHz, CDCl$_3$): δ 7.23–7.24 (m, 2H), 7.31 (t, J = 7.8 Hz, 2H), 7.37 (t, J = 7.2 Hz, 1H), 7.44–7.49 (m, 5H), 8.32 (s, 1H); ^{13}C NMR (150 MHz, CDCl$_3$): δ 125.8, 126.4, 128.6, 128.7, 129.5, 129.98, 130.04, 134.6, 144.9, 153.3; IR (KBr): 3111, 3053, 2921, 1721, 1598, 1555, 1507, 1468, 1389, 1214, 1072, 1017, 957, 770, 692, 568 cm^{-1}; HRMS (ESI): calcd. for $C_{14}H_{12}N_3^+$ [M + H$^+$] 222.1026; found 222.1032.

*3-(4-Methoxyphenyl)-4-phenyl-4H-1,2,4-triazole (**2b**)*. White solid; yield 88 mg, 70%; mp 130–132 °C (Lit[30b] mp 141.5–142 °C, Yield 33%); ^{1}H NMR (600 MHz, DMSO-d_6): δ 3.74 (s, 3H), 6.92 (d, J = 9.0 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 7.37–7.38 (m, 2H), 7.50–7.51 (m, 3H), 8.80 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 55.7, 114.5, 119.3, 126.6, 129.6, 130.2, 130.3, 135.2, 145.7, 152.6, 160.7; IR (KBr): 3115, 2927, 2850, 1613, 1502, 1469, 1379, 1254, 1209, 1174, 1024, 835, 769, 693, 563 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{14}N_3O^+$ [M + H$^+$] 252.1131; found 252.1135.

*4-Phenyl-3-(p-tolyl)-4H-1,2,4-triazole (**3b**).* Light yellow solid; yield 86 mg, 73%; mp 163–165 °C (Lit[30b] mp 165.5–166 °C, Yield 35%); ^{1}H NMR (600 MHz, CDCl$_3$): δ 2.27 (s, 3H), 7.05 (d, J = 7.8 Hz, 2H), 7.17–7.18 (m, 2H), 7.28 (d, J = 7.8 Hz, 2H), 7.40–7.42 (m, 3H), 8.24 (s, 1H).; ^{13}C NMR (150 MHz, CDCl$_3$): δ 21.4, 123.5, 125.8, 128.6, 129.3, 129.5, 130.0, 134.8, 140.1, 144.7, 153.3; IR (KBr): 3108, 2924, 1596, 1502, 1474, 1452, 1383, 1202, 1183, 1087, 1011, 954, 822, 769, 729, 695, 664 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{14}N_3^+$ [M + H$^+$] 236.1182; found 236.1195.

*3-(3-Bromophenyl)-4-phenyl-4H-1,2,4-triazole (**4b**).* Light brown solid; yield 107 mg, 71%; mp 150–152 °C; ^{1}H NMR (600 MHz, CDCl$_3$): δ 7.17 (t, J = 7.8 Hz, 1H), 7.24 (d, J = 7.2 Hz, 2H), 7.30 (d, J = 7.2 Hz, 1H), 7.49–7.54 (m, 4H), 7.70 (s, 1H), 8.34 (s, 1H); ^{13}C NMR (150 MHz, CDCl$_3$): δ 122.8, 125.9, 127.1, 128.4, 129.9, 130.2, 130.3, 131.7, 133.1, 134.4, 145.1, 151.9; IR (KBr): 2923, 1636, 1597, 1502, 1445, 1379, 1202, 1071, 1018, 790, 767, 695, 683 cm^{-1}; HRMS (ESI): calcd. for $C_{14}H_{11}{}^{79}BrN_3^+$ [M + H$^+$] 300.0131; found 300.0139.

*3-(4-Chlorophenyl)-4-phenyl-4H-1,2,4-triazole (**5b**).* White solid; yield 84 mg, 66%; mp 165–168 °C (Lit[30b] mp 176–176.5 °C, Yield 34%); ^{1}H NMR (600 MHz, CDCl$_3$): δ 7.24–7.26 (m, 2H), 7.30 (d, J = 7.8 Hz, 2H), 7.40 (d, J = 8.4 Hz, 2H), 7.50–7.52 (m, 3H), 8.33 (s, 1H); ^{13}C NMR (150 MHz, CDCl$_3$): δ 125.0, 125.9, 129.1, 129.9, 130.0, 130.3, 134.6, 136.4, 145.1, 152.4; IR (KBr): 3106, 2923, 2853, 1595, 1569, 1502, 1467, 1453, 1406, 1380, 1205, 1094, 1083, 1016, 956, 831, 773, 740, 728, 696, 664 cm^{-1}; HRMS (ESI): calcd. for $C_{14}H_{11}{}^{35}ClN_3^+$ [M + H$^+$] 256.0636; found 256.0631.

*3-Phenyl-4-(p-tolyl)-4H-1,2,4-triazole (**6b**).* White solid; yield 81 mg, 69%; mp 144–147 °C (Lit[30c] mp 151 °C, Yield 57%); ^{1}H NMR (600 MHz, CDCl$_3$): δ 2.38 (s, 3H), 7.07 (d, J = 7.8 Hz, 2H), 7.21 (d, J = 8.4 Hz, 2H), 7.27 (t, J = 7.8 Hz, 2H), 7.33 (t, J = 7.2 Hz, 1H), 7.43 (d, J = 7.8 Hz, 2H), 8.25 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.3, 125.7, 126.6, 128.67, 128.72, 130.0, 130.7, 132.2, 139.8, 145.0, 153.3; IR (KBr): 3109, 3063, 2921, 1515, 1495, 1467, 1442, 1390, 1284, 1198, 1073, 1016, 822, 775, 716, 696, 664 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{14}N_3^+$ [M + H$^+$] 236.1182; found 236.1175.

*3,4-Di-p-tolyl-4H-1,2,4-triazole (**7b**).* White solid; yield 97 mg, 78%; mp 192–194 °C (Lit[30d] Yield 59%); ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.30 (s, 3H), 2.39 (s, 3H),7.07–7.09 (m, 4H), 7.22 (d, J = 7.8 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 8.23 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.1, 21.3, 123.6, 125.5, 128.4, 129.2, 130.4, 132.1, 139.6, 139.9, 144.8, 153.2; IR (KBr): 3116, 3033, 2920, 1612, 1517, 1474, 1385, 1206, 1037, 1008, 956, 731, 668 cm^{-1}; HRMS (ESI): calcd. for $C_{16}H_{16}N_3^+$ [M + H$^+$] 250.1339; found 250.1335. $C_{16}H_{15}N_3$, crystal dimensions 0.41 x 0.37 x 0.24 mm, M_r = 249.31, Monoclinic, space group P21/c, a =5.9017(2), b = 14.1916(4), c = 16.0475(4) Å, α = 90 °, β = 92.732(2) °, γ = 90 °, V = 1342.52(7) Å^3, Z = 4, ρ_{calcd} = 1.234 g/cm^3, μ = 0.075 mm^{-1}, F(000) = 528.0, reflection collected / unique = 3295 / 2384, refinement method = full-matrix least-squares on F^2, final R indices [$I > 2\sigma(I)$]: R_1 = 0.0454, wR_2 = 0.1489, R indices (all data): R_1 = 0.0653, wR_2 = 0.1631, goodness of fit = 1.121. CCDC-1054230 for 3,4-Di-*p*-tolyl-4*H*-1,2,4-triazole (7b) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

*3-(3,4-Dimethoxyphenyl)-4-(p-tolyl)-4H-1,2,4-triazole (**8b**).* Light brown liquid; yield 106 mg, 72%; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.37 (s, 3H), 3.68 (s, 3H), 3.80 (s, 3H), 6.69 (d, J = 8.4 Hz, 1H), 6.83 (d, J = 8.4 Hz, 1H), 7.08 (d, J = 7.2 Hz, 3H), 7.22 (d, J = 7.8 Hz, 2H), 8.23 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.3, 55.9, 56.0, 110.9, 111.7, 119.0, 121.5, 125.9, 130.6, 132.4, 139.8, 144.2, 148.9, 150.4, 153.6; IR (KBr): 3120, 2925, 1610, 1517, 1244, 1174, 1141, 1022, 871, 820, 767, 733, 669, 550 cm^{-1}; HRMS (ESI): calcd. for $C_{17}H_{18}N_3O_2^+$ [M + H$^+$] 296.1394; found 296.1390.

*3-(4-Chlorophenyl)-4-(p-tolyl)-4H-1,2,4-triazole (**9b**)*. Light brown solid; yield 100 mg, 74%; mp 163–166 °C (Lit[30e] mp 174–176 °C, Yield 40%); ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.41 (s, 3H), 7.08 (d, *J* = 8.4 Hz, 2H), 7.25–7.28 (m, 4H), 7.39 (d, *J* = 7.2 Hz, 2H), 8.27 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.3, 125.0, 125.6, 128.9, 129.8, 130.7, 131.8, 136.1, 140.0, 145.1, 152.3; IR (KBr): 3108, 3035, 2920, 1602, 1569, 1516, 1463, 1407, 1384, 1318, 1207, 1095, 1015, 1008, 956, 859, 843, 817, 733, 669 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{13}{}^{35}ClN_3^+$ [M + H$^+$] 270.0793; found 270.0799.

*3-(4-Fluorophenyl)-4-(p-tolyl)-4H-1,2,4-triazole (**10b**)*. White solid; yield 90 mg, 71%; mp 127–129 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.44 (s, 3H), 7.02 (t, *J* = 8.4 Hz, 2H),7.11 (d, *J* = 7.8 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.46–7.48 (m, 2H), 8.32 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.3, 115.9 (d, *J* = 21.8 Hz), 122.8, 125.6, 130.7 (d, *J* = 6.5 Hz), 132.0, 140.0, 145.5, 153.3, 163.7 (d, *J* = 249.3 Hz); IR (KBr): 3108, 3059, 2923, 1605, 1518, 1469, 1386, 1319, 1226, 1209, 1182, 1086, 1010, 852, 814, 736, 670, 627 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{13}FN_3^+$ [M + H$^+$] 254.1088; found 254.1085.

*4-(2-Methoxyphenyl)-3-(p-tolyl)-4H-1,2,4-triazole (**11b**)*. Light yellow solid; yield 96 mg, 72%; mp 137–139 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.26 (s, 3H), 3.59 (s, 3H), 6.94–6.98 (m, 2H). 7.03 (d, *J* = 7.8 Hz, 2H), 7.10 (d, *J* = 7.8 Hz, 1H), 7.28 (d, *J* = 7.8 Hz, 2H), 7.38–7.41 (m, 1H), 8.17 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.4, 55.7, 112.6, 121.1, 123.6, 124.2, 127.9, 128.1, 129.2, 131.2, 139.2, 145.2, 153.9, 154.1; IR (KBr): 3084, 3021, 2921, 1603, 1513, 1489, 1468, 1290, 1262, 1208, 1024, 822, 751, 739, 665, 529 cm^{-1}; HRMS (ESI): calcd. for $C_{16}H_{16}N_3O^+$ [M + H$^+$] 266.1288; found 266.1302.

*3-(4-Butoxyphenyl)-4-(4-butylphenyl)-4H-1,2,4-triazole (**12b**)*. Light brown solid; yield 135 mg, 77%; mp 59–61 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.85–0.91 (m, 6H), 1.30 (sextet, *J* = 7.8 Hz, 2H), 1.40 (sextet, J = 7.2 Hz, 2H), 1.55 (quintet, J = 7.2 Hz, 2H), 1.66 (quintet, J = 7.8 Hz, 2H), 2.62 (t, J = 7.2 Hz, 2H), 3.94 (t, J = 6.6 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 7.8 Hz, 2H), 7.28–7.32 (m, 4H), 8.74 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 13.6, 13.7, 18.7, 21.7, 30.7, 32.9, 34.3, 67.3, 114.4, 118.8, 125.9, 129.5, 129.8, 132.3, 143.6, 145.3, 152.1, 159.7; IR (KBr): 2957, 2929, 2871, 1613, 1515, 1466, 1385, 1288, 1251, 1177, 1026, 836, 737, 568 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{28}N_3O^+$ [M + H$^+$] 350.2227; found 350.2239

3-(3,4-Dimethoxyphenyl)-4-(3,4-dimethylphenyl)-4H-1,2,4-triazole ***(13b)***. Light brown gummy; yield 116 mg, 75%; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.19 (s, 3H), 2.25 (s, 3H), 3.67 (s, 3H), 3.78 (s, 3H), 6.67 (d, J = 8.4 Hz, 1H), 6.81–6.83 (m, 1H), 6.89–6.90 (m, 1H), 6.97 (s, 1H), 7.12 (s, 1H), 7.15 (d, J = 7.8 Hz, 1H), 8.19 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 19.6, 19.8, 55.8, 55.9, 110.9, 111.6, 118.9, 121.4, 123.4, 126.8, 130.9, 132.5, 138.4, 138.7, 145.0, 148.8, 150.3, 153.1; IR (KBr): 2928, 2848, 1609, 1498, 1259, 1141, 1023, 862, 819, 730, 659, 593 cm^{-1}; HRMS (ESI): calcd. for $C_{18}H_{20}N_3O_2^+$ [M + H$^+$] 310.1550; found 310.1542.

4-(4-Bromophenyl)-3-phenyl-4H-1,2,4-triazole ***(14b)***. White solid; yield 111 mg, 74%; mp 219–222 ^{o}C (Lit[30c] mp 214–216 ^{o}C, Yield 60%); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.08 (d, J = 8.4 Hz, 2H), 7.27–7.30 (m, 2H), 7.34–7.39 (m, 3H), 7.54-7.56 (m, 2H)

, 8.26 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 123.6, 126.1, 127.3, 128.8, 128.9, 130.3, 133.3, 133.7, 145.0, 153.7; IR (KBr): 3126, 3065, 3034, 1551, 1497, 1468, 1388, 1240, 1200, 1067, 1014, 838, 818, 707, 687, 662 cm^{-1}; HRMS (ESI): calcd. for $C_{14}H_{11}{}^{79}BrN_3^+$ [M + H$^+$] 300.0131; found 300.0125.

4-(4-Bromophenyl)-3-(p-tolyl)-4H-1,2,4-triazole ***(15b)***. White solid; yield 127 mg, 81%; mp 231–233 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.34 (s, 3H), 7.09 (d, J = 8.4 Hz, 2H), 7.13 (d, J = 7.8 Hz, 2H), 7.31 (d, J = 7.8 Hz, 2H), 7.58 (d, J = 9.0 Hz, 2H), 8.26 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.5, 119.4, 123.2, 123.5, 127.4, 128.7, 129.6, 133.3, 133.8, 140.5, 144.8, 153.4; IR

(KBr): 3126, 3066, 3036, 2921, 1497, 1475, 1384, 1199, 1068, 1014, 985, 839, 818, 724, 663 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{13}{}^{79}BrN_3^+$ [M + H^+] 314.0287; found 314.0281.

4-(4-Bromophenyl)-3-(4-methoxyphenyl)-4H-1,2,4-triazole ***(16b)***. Light brown solid; yield 114 mg, 69%; mp 169–171 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.76 (s, 3H), 6.81 (d, J = 9.0 Hz, 2H), 7.08 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 9.0 Hz, 2H), 7.55 (d, J = 8.4 Hz, 2H), 8.24 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 55.5, 114.3, 118.4, 123.5, 127.4, 130.3, 133.3, 133.9, 144.4, 153.1, 161.1; IR (KBr): 3424, 3124, 3034, 2929, 1617, 1574, 1498, 1475, 1385, 1294, 1261, 1201, 1175, 1069, 1029, 830, 816, 662, 567 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{13}{}^{79}BrN_3O^+$ [M + H^+] 330.0237; found 330.0249.

4-(4-Bromophenyl)-3-(4-chlorophenyl)-4H-1,2,4-triazole ***(17b)***. Light brown solid; yield 125 mg, 75%; mp 185–187 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.09 (d, 2H, J = 9.0 Hz, 2H), 7.29 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 8.4 Hz, 2H), 8.28 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 124.0, 124.6, 127.4, 129.0, 129.3 130.0, 133.6, 136.6, 144.4, 152.9; IR (KBr): 2927, 2863, 1723, 1494, 1280, 1197, 1068, 1012, 826, 662 cm^{-1}; HRMS (ESI): calcd. for $C_{14}H_{10}{}^{79}Br^{35}ClN_3^+$ [M + H^+] 333.9741; found 333.9746.

3,4-bis(4-Bromophenyl)-4H-1,2,4-triazole ***(18b)***. White solid; yield 112 mg, 59%; mp 242–244 °C (Lit[30c] mp 225–226 °C, Yield 77%); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.09 (d, J = 9.0 Hz, 2H), 7.30 (d, J = 9.0 Hz, 2H), 7.47 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 8.4 Hz, 2H), 8.29 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 124.0, 125.0, 125.1, 127.4, 130.2, 132.2, 133.5, 133.6, 144.9, 152.4; IR (KBr): 3121, 3034, 2920, 1599, 1567, 1495, 1459, 1405, 1380, 1199, 1067, 1013, 841, 821, 722, 664 cm^{-1}; HRMS (ESI): calcd. for $C_{14}H_{10}{}^{79}Br_2N_3^+$ [M + H^+] 377.9236; found 377.9246.

4-(4-Chlorophenyl)-3-(p-tolyl)-4H-1,2,4-triazole ***(19b)***. White solid; yield 97 mg, 72%; mp 194–196 °C (Lit[30e] mp 201–203 °C, Yield 57%); ^{1}H NMR (600 MHz, DMSO-d_6): δ 2.30 (s, 3H), 7.21 (d, J = 7.8 Hz, 2H), 7.27 (d, J = 7.8 Hz, 2H), 7.41 (d, J = 9.0 Hz, 2H), 7.58 (d, J = 8.4 Hz, 2H), 8.84(s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 21.3, 124.0, 128.4, 128.9, 129.7, 130.2, 133.9, 134.2, 140.0, 145.8, 152.7; IR (KBr): 3434, 3040, 2922, 1500, 1476, 1385, 1199, 1093, 1085, 1015, 840, 819, 726, 665, 568 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{13}{}^{35}ClN_3^+$ [M + H^+] 270.0793; found 270.0780.

3,4-Bis-(4-chlorophenyl)-4H-1,2,4-triazole ***(20b)***. White solid; yield 106 mg, 73%; mp 165–167 °C (Lit[30e] mp 184–186 °C, Yield 40%); ^1H NMR (600 MHz, $CDCl_3$): δ 7.15 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 9.0 Hz, 2H), 8.26 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 124.6, 127.1, 129.2, 130.0, 130.5, 132.9, 135.9, 136.6, 145.1, 152.9; IR (KBr): 3043, 2924, 1602, 1554, 1497, 1408, 1199, 1093, 1014, 833, 729, 565 cm^{-1}; HRMS (ESI): calcd. for $C_{14}H_{10}{}^{35}Cl_2N_3^+$ [M + H^+] 290.0246; found 290.0241.

4-(4-Butylphenyl)-3-(furan-2-yl)-4H-1,2,4-triazole ***(22b)***. Brown gummy; yield 90 mg, 67%; ^1H NMR (600 MHz, $CDCl_3$): δ 0.91 (t, J = 7.2 Hz, 3H), 1.34 (sextet, J = 7.8 Hz, 2H), 1.61 (quintet, J = 7.2 Hz, 2H), 2.66 (t, J = 7.8 Hz, 2H), 6.34 (s, 2H), 7.18 (d, J = 7.8 Hz, 2H), 7.28 (d, J = 7.8 Hz, 2H), 7.38 (s, 1H), 8.18 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 14.0, 22.4, 33.5, 35.4, 111.5, 112.0, 126.1, 129.8, 131.7, 142.6, 144.3, 145.4, 147.0, 153.4; IR (KBr): 2959, 2864, 2836, 1602, 1561, 1516, 1464, 1407, 1275, 1205, 1097, 1015, 904, 835, 668, 569 cm^{-1}; HRMS (ESI): calcd. for $C_{16}H_{18}N_3O^+$ [M + H^+] 268.1444; found 268.1452.

5-(2,6-dichlorophenyl)-N-phenyl-1,3,4-thiadiazol-2-amine ***(23c)***. White solid; yield 98 mg, 61%; mp 228–230 °C; ^1H NMR (600 MHz, DMSO-d_6): δ 7.02 (t, J = 7.2 Hz, 1H), 7.37 (t, J = 7.8 Hz, 2H), 7.58 (t, J = 7.8 Hz, 1H), 7.64–7.69 (m, 4H), 10.63 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 117.6, 122.2, 128.2, 128.6, 129.1, 132.8, 135.3, 140.3, 150.6, 166.2; IR (KBr): 3439, 3245, 3061, 2923, 1602, 1571, 1501, 1455, 1430, 1190, 1109, 979, 789, 752, 693 cm^{-1}; HRMS (ESI): calcd. for $C_{14}H_{10}Cl_2N_3S^+$ [M + H^+] 321.9967; found 321.9981.

3-(4-chlorophenyl)-4-(2,6-dimethylphenyl)-4H-1,2,4-triazole ***(24b)***. White solid; yield 38 mg, 27%; mp 181–183 °C; ^1H NMR (600 MHz, $CDCl_3$): δ 1.97 (s, 6H), 7.21 (d, J = 7.2 Hz, 2H), 7.27 (d, J = 6.6 Hz, 2H), 7.35 (t, J = 7.2 Hz, 1H), 7.41 (d, J = 7.8 Hz, 2H), 8.18 (s, 1H); ^{13}C NMR (150

MHz, $CDCl_3$): δ 17.9, 125.3, 128.2, 129.2, 129.3, 130.3, 132.9, 135.4, 136.3, 144.6, 151.8; IR (KBr): 3436, 3118, 3057, 2920, 2853, 1671, 1571, 1488, 1464, 1408, 1368, 1197, 1094, 1010, 983, 849, 816, 784, 731, 669 cm^{-1}; HRMS (ESI): calcd. for $C_{16}H_{15}ClN_3^+$ [M + H^+] 284.0949; found 284.0942.

5-(4-chlorophenyl)-N-(2,6-dimethylphenyl)-1,3,4-thiadiazol-2-amine ***(24c)***. White solid; yield 65 mg, 41%; mp 229–231 °C (Lit[29h] mp 231–234 °C, Yield 54%); ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.39 (s, 3H), 7.16-7.20 (m, 3H), 7.33 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 7.8 Hz, 2H), 9.53 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 18.4, 128.0, 128.3, 129.2, 129.25, 129.34, 129.7, 135.4, 136.6, 138.8, 156.5, 172.5; IR (KBr): 3436, 3157, 2920, 2852, 1596, 1555, 1505, 1467, 1427, 1262, 1212, 1089, 1014, 981, 832, 785, 642 cm^{-1}; HRMS (ESI): calcd. for $C_{16}H_{15}ClN_3S^+$ [M + H^+] 316.0670; found 316. 0682.

AUTHOR INFORMATION

Corresponding Author

*E mail: patel@iitg.ernet.in.

ACKNOWLEDGMENT

B. K. P acknowledges the support of this research by the Department of Science and Technology (DST) (SB/S1/OC-53/2013), New Delhi, and the Council of Scientific and Industrial Research (CSIR) (02(0096)/12/EMR-II). WA and SG thank CSIR for fellowship.

Supporting Information Available

Deuterium exchange experiment and spectral data for all compounds, X-ray crystallographic data (CIF files). This material is available free of charge *via* the Internet at http://pubs.acs.org.

REFERENCES

1. (a) Yeung, C. S.; Dong, V. M. *Chem. Rev*. **2011**, *111*, 1215. (b) Liu, C.; Zhang, H.; Shi, W.; Lei, A. *Chem. Rev*. **2011**, *111*, 1780. (c) Lie, B. -J.; Shi, Z. -J. *Chem. Soc. Rev*. **2012**, *41*, 5588.
2. (a) Metal-Catalyzed Cross-Coupling Reactions: Diederich, F.; Stang, P. J.; Ed.; Wiley-VCH: Weinheim, 1998. (b) Handbook of C-H transformations. Ed. G. Dyker, Wiley-VCH, Weinheim, 2005. (c) Topics in Current Chemistry, Ed.; J.-Q. Yu and Z. Shi, Springer, 2010, vol. 292. (d) Shilov, A. E.; Shul'pin, G. B. *Chem. Rev.* **1997**, *97*, 2879. (e) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (f) Ackermann, L. *Chem Rev.* **2011**, *111*, 1315. (g) Sun, C. -L.; Li, B. -J.; Shi, Z. -J. *Chem. Commun*. **2010**, *46*, 677. (h) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Sottocornola, S. *Chem. Rev*. **2007**, *107*, 5318. (i) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174. (j) Jazzar, R.; Hitce, J.; Renaudat, A.; Sofack-Kreutzer, J.; Baudoin, O. *Chem. Eur. J*.; **2010**, *16*, 2654. (k) Giri, R.; Shi, B. -F.; Engle, K. M.; Maugel, N.; Yu, J. -Q. *Chem. Soc. Rev.* **2009**, *38*, 3242. (l) Chem, X.; Enhle, K. M.; Wanh, D. -H.; Yu, J. -Q. *Angew. Chem. Int. Ed.* **2009**, *48*, 5094. (m) Thansandote, P.; Lautens, M. *Chem. Eur. J.* **2009**, *15*, 5874. (n) Balcells, D.; Clot, E.; Eisenstein, O. *Chem. Rev.* **2010**, *110*, 749. (o) Beck, E. M.; Gaunt, M. J. *Top. Curr. Chem.* **2010**, *292*, 85. (p) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res*. **2009**, *42*, 1074. (q) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev*. **2010**, *110*, 624. (r) Díaz-Requejo, M. M.; Pérez, P. J. *Chem. Rev*. **2008**, *108*, 3379. (s) Shilov, A. E.; Shul'pin, G. B. *Chem. Rev*. **1997**, *97*, 2879. (t) Beletskaya, I. P.; Ananikov, V. P. *Chem. Rev.* **2011**, *111*, 1596. (u) Wencel-Delord, J.; Dröge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40,* 4740.
3. (a) Qian, B.; Guo, S.; Shao, J.; Zhu, Q.; Yang, L.; Xia, C.; Huang, H. *J. Am. Chem. Soc*. **2010**, *132*, 3650. (b) Aydin, J.; Conrad, C. S.; Szabó, K. J. *Org. Lett*. **2008**, *10*, 5175. (c) Aydin, J.; Szabo, K. J. *Org. Lett*. **2008**, *10*, 2881. (d) Fukutani, T.; Umeda, N.; Hirano, K.; Satoh, T.; Miura, M. *Chem. Commun*. **2009**, 5141. (e) Tsai, A. S.; Tauchert, M. E.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2011**, *133*, 1248. (f) Yotphan, S.; Bergmann, R. G.; Ellman, J. A. *Org. Lett*. **2009**, *11*, 1511. (g) Guin, S.; Ghosh, S.; Rout, S. K.; Banerjee, A.; Patel, B. K. *Org. Lett*. **2011**, *13*, 5976. (h)

Noto, R.; Gruttadauria, M.; Meo, P. L.; Frenna, V.; Werber, G. *J. Het. Chem*. **1995**, *32*, 1277. (i) Bluhm, M. E.; Ciesielski, N.; Görls, H.; Döring, M. *Angew. Chem. Int. Ed*. **2002**, *41*, 2962.

4. (a) Guru, M. M.; Ali, M, A.; Punniyamurthy, T. *Org. Lett*. **2011**, *13*, 1194. (b) Guru, M. M.; Ali, M.; Punniyamurthy, T. *J. Org. Chem*. **2011**, *76*, 5295. (c) Nakamura, I.; Araki, T.; Zhang, D.; Kudo, Y.; Kwon, E.; Terada, M. *Org. Lett*. **2011**, *13*, 3616.
5. Wang, H.; Wang, Y.; Peng, C.; Zhang, J.; Zhu, Q. *J. Am. Chem. Soc.* **2010**, *132*, 13217.
6. (a) Jang, Y. H.; Youn, S. W. *Org. Lett*. **2014**, *16*, 3720. (b) Samanta, R.; Bauer, J. O.; Strohmann, C.; Antonchick, A. P. *Org. Lett*. **2012**, *14*, 5518. (c) Chi, Y.; Zhang, W.-X.; Xi, Z. *Org. Lett*. **2014**, *16*, 6274.
7. (a) Burch, H. A.; Smith, W. O. *J. Med. Chem.* **1966**, *9*, 405. (b) Foroumadi, A.; Mansouri, S.; Kiani, Z.; Rahmani, A. *Eur. J. Med. Chem.* **2003**, *38*, 851. (c) Ram, V. J.; Mishra, L.; Pandey, N. H.; Kushwaha, D. S.; Pieters, L. A. C.; Vlietinck, A. J. *J. Heterocycl. Chem.* **1990**, *27*, 351. (d) Ergenc, N.; Ilhan, E.; Ötük, G. *Pharmazie* **1992**, *47*, 59. (e) Plech, T.; Wujec, M.; Siwek, A.; Kosikowska, U.; Malm, A. *Eur. J. Med. Chem*. **2011**, *46*, 241.
8. (a) Kalyoncuoğlu, N.; Rollas, S.; Sür-Altiner, D.; Yegenoğlu, Y.; Anğ, Ö. *Pharmazie* **1992**, *47*, 796. (b) Rollas, S.; Kalyoncuoğlu, N.; Sür-Altiner, D.; Yegenoğlu, Y. *Pharmazie* **1993**, *48*, 308.
9. Dogan, H. N.; Duran, A.; Rollas, S. *Indian J. Chem. Sect. B*. **2005**, *44***,** 2301.
10. Amir, M.; Kumar, S. *Acta Pharm*. **2007**, *57***,** 31.
11. Küçükgüzel, I.; Tatar, E.; Küçükgüzel, Ş. G.; Rollas, S.; Clercq, E. De. *Eur. J. Med. Chem*. **2008**, *43***,** 381.
12. Mir, I.; Siddiqui, M. T.; Comrie, A. *Tetrahedron* **1970**, *26*, 5235.
13. Kane, J. M.; Staeger, M. A.; Dalton, C. R.; Miller, F. P.; Dudley, M. W.; Ogden, A. M. L.; Kehne, J. H.; Ketteler, H. J.; McCloskey, T. C. ; Senyah, Y.; Chmieleweski, P. A.; Miller, J. A. *J. Med. Chem.* **1994**, *37,* 125.
14. Kane, J. M.; Dudley, M. K.; Sorensen, S. M.; Miller, F. P. *J. Med. Chem*. **1988,** *31,* 1253.

15. (a) Liu, S.; Qian, Xh.; Song, G.; Chen, J.; Chen, W. *J. Florine Chem.* **2000**, *105,* 111. (b) Mullican, M. D.; Wilson, M. W.; Conner, D. T.; Kostlan, C. R.; Schrier, D. J.; Dyer, R. D. *J. Med. Chem.* **1993**, *36*, 1090. (c) Hoggarth, E. *J. Chem. Soc.* **1949**, 1163. (d) Sandstrom, J.; Wennrbeck, I. *Acta. Chem. Scand.* **1966**, *20***,** 57. (e) Kane, J. M.; Dudley, M. W.; Sorensen, S. M.; Miller, F. P. *J. Med. Chem.*, **1988**, *31***,** 1253. (f) Dogan, H. N.; Rolla, S.; Erdeniz, H. *IL Farmaco*, **1998**, *53***,** 462. (g) Vashi, B. S.; Mehta, D. S.; Shah, V. H. *Indian J. Chem.*, **1996**, *35B,* 111. (h) Rigo, B.; Couturier, D. *J. Heterocyclic Chem.*, **1989**, *26,* 1723. (i) Colaceska-Ragenovic, K.; Dimova, V.; Kakurinov, V.; Molnar Gabor, D. *J. Heterocyclic Chem.*, **2003**, *40,* 905. (j) Gulerman, N. N.; Dogan, H. N.; Rollas, S.; Johonsson, C.; Celike, C. *IL Farmaco*, **2001**, *56,* 953. (k) Gulerman, N. N.; Dogan, H. N.; Rollas, S.; Johonsson, C.; Celike, C. *IL Farmaco*, **2001**, *56,* 953. (l) Rostamizadeh, S.; Mollahoseini, K.; Moghadasi, S. *Phosphorus, Sulfur Silicon Relat. Elem.* **2006**, *181*, 1839.

16. Talawar, M. B.; Bennur, S. C.; Kankanwadi, S. K.; Patil, P. A. *Indian J. Pharm. Sci.* **1995**, *57***,** 194.

17. (a) Hoggarth, E. *J. Chem. Soc.* **1949**, 1160. (b) Durant, G. J. *J. Chem. Soc. C*, **1967**, 92.

18. Kane, J. M. *Synthesis* **1987**, 912.

19. (a) Patani, G. A.; LaVoie, E. J. *Chem. Rev*. **1996**, *96*, 3147. (b) Kucukguzel, L.; Kucukguzel, S. G.; Rollas, S.; Kiraz, M. *Bioorg. Med. Chem. Lett*. **2001**, *11*, 1703. (c) Prakash, O.; Hussain, K.; Aneja, D. K.; Sharma, C.; Aneja, K. R. *Org. Med. Chem. Lett*. **2011**, *1*, 1. (d) Street, L. J.; Baker, R.; Davey,W. B.; Guiblin, A. R.; Jelly, R. A.; Reeve, A. J.; Routledge, H.; Sternfeld, F.;Watt, A. P.; Beer, M. S.; Middlemiss, D. N.; Noble, A. J.; Stanton, J. A.; Scholey, K.; Hargreaves, R. J.; Sohal, B.; Graham, M. I.; Matassat, V. G. *J. Med. Chem*. **1995**, *38*, 1799. (e) Lowe, R. F.; Nelson, J.; Dang, T. N.; Crowe, P. D.; Pahuja, A.; McCarthy, J. R.; Grigoriadis, D. E.; Conlon, P.; Saunders, J.; Chen, C.; Szabo, T.; Chen, T. K.; Bozigian, H. *J. Med. Chem*. **2005**, *48*, 1540.

20. (a) Khadir, A.; Verreault, J.; Averill, D. A. *Arch. Biochem. Biophys*. **1999**, *370*, 163. (b) Ventura, L.; PerezGonzales, J. A.; Ramon, D. *FEMS Microbiol. Lett.* **1997**, *149*, 207. (c) Marino, J. P.;

Fisher, P. W.; Hofmann, G. A.; Kirkpatrick, R. B.; Janson, C. A.; Johnson, R. K.; Ma, C.; Mattern, M.; Meek, T. D.; Ryan, M. D.; Schulz, C.; Smith, W. W.; Tew, D. G.; Tomazek, T. A.; Veber, D. F.; Xiong, W. C.; Yamamoto, Y.; Yamashita, K.; Yang, G.; Thompson, S. K. *J. Med. Chem*. **2007**, *50*, 3777.

21. (a) Naito, Y.; Akahoshi, F.; Takeda, S.; Okada, T.; Kajji, M.; Nishimura, H.; Sigiura, M.; Fukaya, C.; Kagitani, Y. *J. Med. Chem*. **1996**, *39*, 3019. (b) Hartmann, M.; Bauer, H.-J.; Wermann, K. *Biocide Polym*. **1985**, 195. (c) Fauchere, J. -L.; Ortuno, J. C.; Duhault, J.; Boutin, J. A.; Levens, N. European Patent EP 1044970, **2000.**
22. (a) Hitotsuyanagi, Y.; Motegi, S.; Fukaya, H.; Takeya, K. *J. Org. Chem.* **2002**, *67*, 3266. (b) Hitotsuyanagi, Y.; Motegi, S.; Hasuda, T.; Takeya, K. *Org. Lett*. **2004**, *6*, 1111. (c) Borg, S.; Vollinga, R. C.; Labarre, M.; Payza, K.; Terenius, L.; Luthman, K. *J. Med. Chem*. **1999**, *42*, 4331.
23. (a) Brucato, A.; Coppola, A.; Gianguzza, S.; Provenzano, P. M. *Bull. Soc. Ital. Biol. Sper.* **1978**, *54*, 1051. (b) Coffen, D. L.; Fryer, R. I. US Pat. **1974**, 3 849 434. *Chem. Abstr. 82*, 730044v. (c) Shiroki, M.; Tahara, T.; Araki, K. Jap. Pat. **1975**, 75100096; *Chem. Abstr. 84*, 59588k.
24. (a) Bluhm, M. E.; Ciesielski, N.; Görls, H.; Döring, M. *Angew Chem. Int. Ed.* **2002**, *41*, 2962. (b) Basu, A.; Das, G. *Dalton Trans.* **2011**, *40*, 2837. (c) Noto, R.; Meo, P. L.; Gruttadauria, M.; Werber, G. *J. Het. Chem.* **1999**, *36*, 667. (d) de Aquino, T. M.; Liesen, A. P.; da Silva, R. E. A.; Lima, V. T.; Carvalho, C. S.; de Faria, A. R.; de Araújo, J. M.; de Lima, J. G.; Alves, A. J.; de Melo, E. J. T.; Góes, A. J. S. *Bio. Med. Chem*. **2008**, *16*, 446
25. Barun, O.; Ila, H.; Junjappa, H.; Singh, O. M. *J. Org. Chem.* **2000**, *65*, 1583.
26. Sviridov, S. I.; Shorshnev, S. V.; Stepanov, A. E. *Synthesis* **2006**, 156.
27. (a) Gautam, U. K.; Mukherjee, B. *Bull. Mater. Sci*. **2006**, *29*, 1. (b) Chen, C., Li, Q.; Wang, Y.; Li, Y.; Zhong, X. *Front. Optoelectron. China* **2011**, *4*, 150.
28. (a) Sahoo, S. K.; Jamir, L.; Guin, S.; Patel, B. K. *Adv. Synth. Catal.* **2010**, *352*, 2538. (b) Johansen, H. *Acta. Chem. Scand.* **1995**, *49*, 79.

29. (a) Kuśmierza, E.; Siweka, A.; Kosikowskab, U.; Malmb, A.; Plech, T.; Wróbelc, A.; Wujec, M. *Phosphorus, Sulfur Silicon Relat. Elem.* **2014**, *189,* 1539. (b) Abuo-Rahma, G. E. A.A.; Abdel-Aziz, M.; Beshr, E. A.M.; Ali, T. F.S. *Eur. J. Med. Chem.* **2014**, *71*, 185. (c) Malbec, F.; Milcent, R.; Barbier, G. *J. Heterocycl. Chem.* **1984**, *21*, 1689. (d) Senthilvelan, A.; Ramakrishnan, V. T. *Heteroat. Chem.* **2003**, *14*, 269. (e) Pathak, U. S.; Devani, M. B.; Shishoo, C. J.; Shah, S. A. *Indian J. Chem., Sect B.* **1989**, *28B*, 83. (f) Plech, T.; Wujec, M. Majewska, M.; Kosikowska, U.; Malm, A. *Med. Chem. Res.* **2013**, *22*, 2531. (g) Kumudha, D.; Leonard, J.T.; Muthumani, M.; Chidhambaranathan, N.; Kalavathi,T. *Asian J. Pharm. Clin. Res.* **2013**, *6*, 5. (h) Khan, I.; Ali, S.; Hameed, S.; Hasan Rama, N.; Tahir Hussain, M.; Wadood, A.; Uddin, R.; Ul-Haq, Z.; Khan, A.; Ali, S.; Choudhary, M. I. Euro. *J. Med. Chem*. **2010**, *45*, 5200.

30. (a) Chen, X.; Liu, R.; Xu, Y.; Zou, G. *Tetrahedron* **2012**, *68*, 4813. (b) Kevill, D. N.; Park, M. A. *Tetrahedron Lett.* **1978**, *47*, 4629. (c) Korotkikh, N. I.; Kiselev, A. V.; Knishevitsky, A. V.; Raenko, G. F.; Pekhtereva, T. M.; Shvaika, O. P. *Chem. Heterocycl. Compd.* **2005**, *41*, 866. (d) Senthilvelan, A.; Thirumalai, D.; Ramakrishnan, V.T. *Tetrahedron* **2004**, *60*, 851. (e) Ito, S.; Tanaka, Y.; Kakehi, A. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 544.

31. (a) SMART V 4.043 Software for the CCD Detector System; Siemens Analytical Instruments Division: Madison, WI, 1995. (b) SAINT V 4.035 Software for the CCD Detector System; Siemens Analytical Instruments Division: Madison, WI, 1995. (c) Sheldrick, G. M. SHELXL-97, Program for the Refinement of Crystal Structures; University of Göttingen: Göttingen (Germany), 1997.