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A ligand free copper(II) catalyst is as effective as a ligand assisted Pd(II) catalyst towards intramolecular C–S bond formation via C–H functionalization

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ABSTRACT

Copper(I) catalysts are usually ineffective on the other hand Pd(II) catalysts are quite effective in promoting intramolecular sp^2 C–H functionalization (C–S bond formation). Herein, we have developed a ligand assisted Pd(II) catalyzed C–S bond formation via C–H activation from arylthioureas leading to the formation of 2-aminobenzothiazoles for substrates bearing electron donating (EDG) groups in the aryl ring. However without the assistance of ligand this Pd(II) catalyzed reaction is quite unproductive particularly for thioureas possessing strongly electron donating groups in the aryl rings. Interestingly, the ligand free Cu(II) catalyzed oxidative cyclization of arylthioureas are equally effective both for arylthioureas possessing electron donating as well as electron withdrawing groups in the aryl rings.

1. Introduction

2-Aminobenzothiazoles (Hugerschoff product), are obtained from unsymmetrical aryl-sec-alkyl thioureas (Tu) using molecular bromine (or its equivalent) or iodine.[1] Although activated aromatics (substrates possessing electron donating groups) undergo intramolecular aromatic electrophilic substitution to give the Hugerschoff product 2-aminobenzothiazoles[2] but most other substrates gave thioamidoguanidines (Tag) (*anti*-Hugerschoff product)[2a] exclusively via an oxidative dimerization path (path A, Scheme 1). In order to suppress the competitive formation of Hugerschoffs and to give *anti*-Hugerschoff products exclusively a strategy has been developed by our group, wherein the Cu(II) salt promotes an oxidative dimerization (S–S bond formation) of thiourea, which is the essential intermediate for the formation of *anti*-Hugerschoff product (path A, Scheme 1).[3] During the formation of *anti*-Hugerschoff product from aryl-sec-alkyl thiourea (Tu) no C–H activation (C–S bond formation) was observed at room temperature. 2-Halo (–F, –Cl) arylthioureas, which are usually inert toward dehalogenative C–S bond formation gave *anti*-Hugerschoff products via an oxidative dimerization path with redox active Cu(II) salt at room temperature (Path B, Scheme 1).[3] However, at an elevated temperature C–S bond formation leading to the synthesis of 2-aminobenzothiazole was observed using Cu(II) (path C, Scheme 1).[3] The same dehalogenative C–S bond formation was achieved using CuI[4] and CuO nanoparticle[5] in water at an elevated temperature (path C, Scheme 1). Further, it has been observed that Cu(I) prefers a dehalogenative path over C–H activation for the entire range of halogens (–F, –Cl, –Br, –I) (path C, Scheme 1) and in the absence of any 2-halo groups it is unproductive whereas a Pd-catalyzed reaction favors a dehalogenative path for activated halogens (–Br, –I) (path D, Scheme 1) and C–H activation path (C–S bond formation) for less activated halogens (–F, –Cl) (path E, Scheme 1).[6]

Of late transition metal catalyzed C–H functionalization is an exciting area of research, representing an atom-economic and greener prospective, which improves the overall efficacy of synthetic processes. The ubiquitous C–H bonds can now be considered as dormant synthetic equivalents of several reactive functional groups. Among the various transition metal catalysts employed for this process, Pd and Cu are the most well explored ones.[7] Usually Cu catalyzed reactions are preferred due to the cost consideration and better environmental acceptability whereas Pd-catalyzed reactions are superior in spite of high cost due to its efficacy and high turnover numbers.[8]

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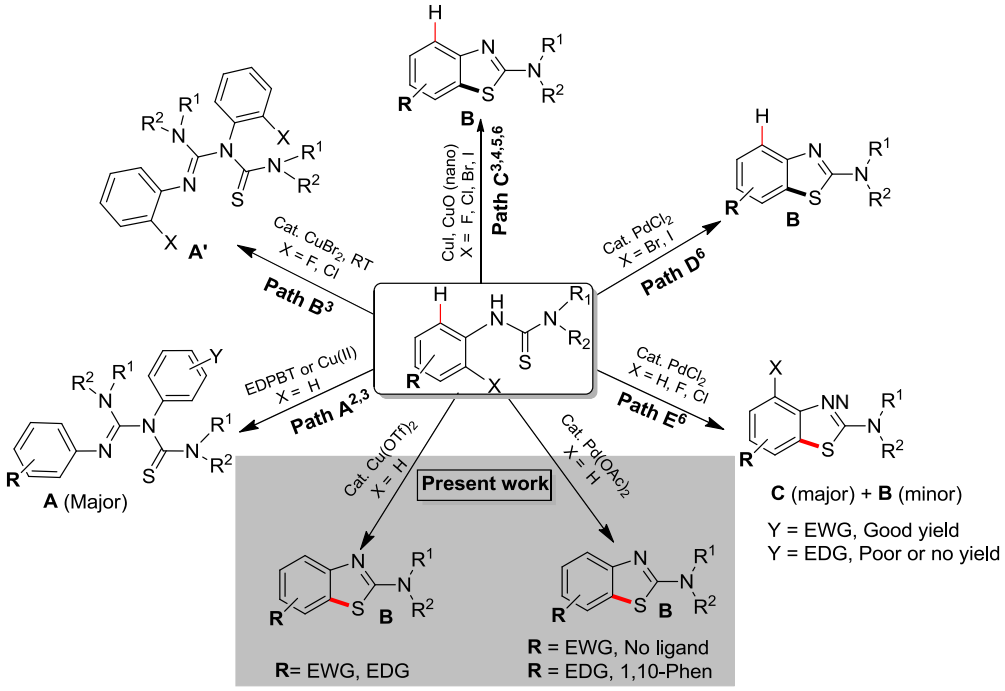


Scheme 1. Fate of Cu and Pd catalyzed reactions of thioureas.

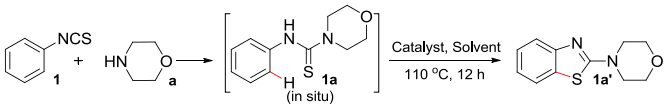
No doubt our Pd(II) catalyzed synthesis of 2-aminobenzothiazole via C–H activation strategy is quite promising (path E, Scheme 1) but the methodology is applicable mostly for substrates possessing electron withdrawing groups (EWG) in the aromatic rings.[6] For substrates possessing strongly electron donating groups, such as –OMe, –OBu the reaction failed to give any product. Batey et al. have made similar observations, i.e., lower yield in case of thioureas possessing electron donating groups and for more activated substrates possessing multiple electron donating groups as in the case of (*m*,*m*-Me, *m*,*m*,*p*-OMe) the desired product was not obtained at all.[9] Two more alternative synthesis of similar scaffold has been achieved via the C–H activation (C–S bond formation) of *o*-aryl sp^2 C–H bond of *N*-arylthioamides using Pd(II) catalyst.[10] Very recently a iron(II) catalyzed synthesis of 2-substituted benzothiazole from *N*-arylbenzothioamide via an oxidative C–H functionalization (C–S bond formation) is reported by Lei et al.[11] Buchwald et al. also demonstrated a $Cu(OAc)_2$-catalyzed synthesis of benzimidazoles from corresponding amines through a C–H activation (C–N bond formation) process.[12] Nagasawa group[13] has reported a copper catalyzed intramolecular C–O bond formation via C–H activation strategy using *N*-arylurea as the precursor in an oxygen atmosphere. Recently, a copper catalyzed intramolecular C–O bond formation strategy has been demonstrated by our group for the synthesis of 1,3,4-oxadiazoles via an imine C–H bond functionalization.[14] Thus, a query arises whether an intramolecular C–S bond formation via C–H functionalization could be achieved from thioureas using environmentally acceptable low cost catalyst, such as copper.

There is no prior report on the synthesis of 2-aminobenzothiazole via a C–H functionalization using cheap and environmentally acceptable catalyst like copper. On the other hand synthesis of 2-aminobenzothiazoles using Pd-catalyzed intramolecular C–S bond formation via C–H functionalization should also be improved and a method should also be developed, which should work for substrates possessing both electron donating as well as electron withdrawing groups. Herein a systematic study has been carried out on the differential selectivity for Cu and Pd catalyzed synthesis of 2-aminobenzothiazole from *N*-arylthiourea following the C–H functionalization strategy.

2. Results and discussion

Among various Cu(II) salts $Cu(OTf)_2$ is the most efficient in promoting intramolecular C–O bond formation via sp^2 C–H bond activation as has been demonstrated by our group as well as by Nagasawa et al.[13,14] Taking cues from these we used $Cu(OTf)_2$ toward the intramolecular C–S bond formation of *N*-arylthiourea (**1a**) via a C–H bond functionalization strategy. Accordingly, *N*-arylthiourea (**1a**) was reacted with $Cu(OTf)_2$ (10 mol %), in DMF the desired product 2-aminobenzothiazole (**1a′**) was obtained in a moderate yield of 40% (Table 1, entry 1). Further, optimizations were carried out to arrive at the best possible yield as shown in Table 1. During the optimization it was observed that the reaction did not proceed in solvents like acetone, 1,4-dioxane, acetonitrile

Table 1
Screening of reaction conditions



Entry	Catalyst (mol %)	Solvent	Yield (%)
1	$Cu(OTf)_2$ (10.0)	DMF	40
2	$Cu(OTf)_2$ (10.0)	Acetone	No reaction
3	$Cu(OTf)_2$ (10.0)	1,4-Dioxane	No reaction
4	$Cu(OTf)_2$ (10.0)	CH_3CN	No reaction
5	$Cu(OTf)_2$ (10.0)	DMSO	25
6	$Cu(OTf)_2$ (10.0)	Toluene	65
7	$Cu(OTf)_2$ (20.0)	Toluene	68
8	$CuCl_2$ (10.0)	Toluene	No reaction
9	$CuBr_2$ (10.0)	Toluene	No reaction
10	$Cu(OAc)_2$ (20.0)	Toluene	20
11	**$Cu(OTf)_2$ (10.0)**	**Toluene**	**85**[a]

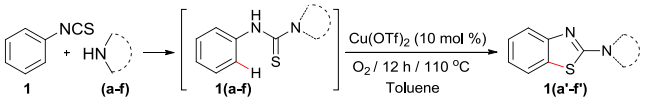
Bold value signifies the most optimized condition.
[a] Reaction performed under O_2 atmosphere.

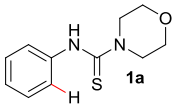
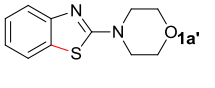
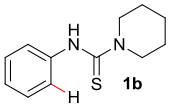
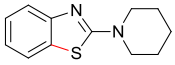
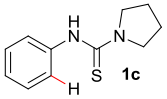
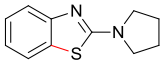
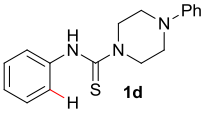
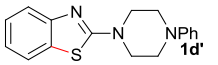
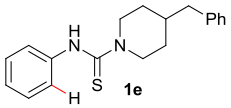
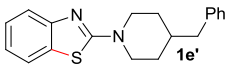
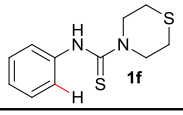
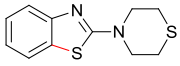
(Table 1, entries 2, 3, and 4). The use of polar aprotic solvent, such as DMSO gave a poor yield of the product (25%) (Table 1, entry 5). Switching the solvent to toluene the desired product (**1a**′) was obtained in an improved yield of 65% (Table 1, entry 6). No significant improvement was observed in the product yield when the catalyst loading was increased to 20 mol % (68%) (Table 1, entry 7). The reactions did not provide the desired product 2-aminobenzothiazole (**1a**′) when other Cu(II) salts, such as $CuCl_2$ and $CuBr_2$ were used (Table 1, entries 8 and 9). It is pertinent to mention that the analogous substrate with $CuBr_2$ gave thioaminoguanidines[3] however under this reaction conditions the same product is not formed, which is probably due to the difference in the reaction conditions and the quantity of $CuBr_2$ used. Although the desired transformation could be achieved using $Cu(OAc)_2$ but the yield was poor (20%) (Table 1, entry 10). By carrying out the reaction at 110 °C under an oxygen atmosphere in toluene using $Cu(OTf)_2$ (10 mol %) as the catalyst the yield improved upto 85% (Table 1, entry 11). No further improvement in the yield was observed when the temperature was increased above 110 °C but the yield decreased with decrease in the reaction temperature.

Thioureas generated in situ by reacting phenyl isothiocyanate (**1**) and secondary amines, such as morpholine (**a**), piperidine (**b**), pyrrolidine (**c**), *N*-substituted piperazine (**d**), 4-benzylpiperidin (**e**), and thiomorpholine (**f**) all provided moderate to good yields of their desired products (**1a**′–**1f**′) via this novel C–H activation (C–S bond formation) protocol as shown in Table 2. On the other hand thioureas generated in situ by reacting phenyl isothiocyanate (**1**) and primary amines like, benzyl amine, aniline etc. did not provide desired products under this reaction conditions. This is possibly because of the competitive co-ordination of the second nitrogen to metal thereby preventing *o*-metalation, which is essential for this transformation.

Further, the scope of this protocol was examined using varieties of *N*-arylthioureas derived from different aryl isothiocyanates and morpholine as the secondary amine (Table 3). Thioureas possessing electron withdrawing and electron donating substituents in the aromatic core all provided their desired products in good to excellent yields (Table 3). For *N*-arylthiourea possessing electron withdrawing substituents in the aromatic ring, such as *m*-Cl (**2a**),

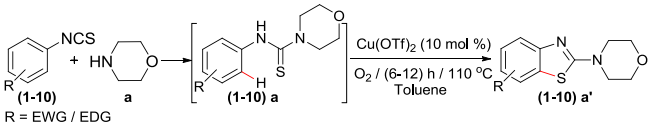
Table 2
Cu catalyzed synthesis of 2-aminobenzothiazoles.from aryl-sec-alkyl thioureas

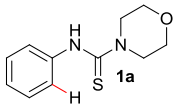
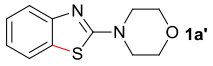
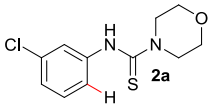
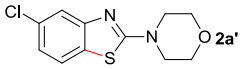
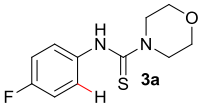
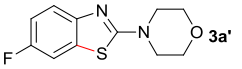
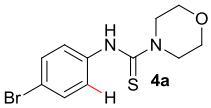
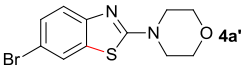
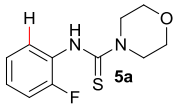
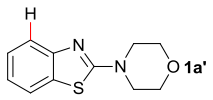
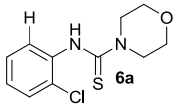
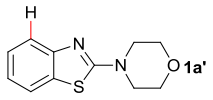
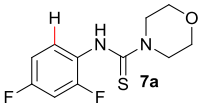
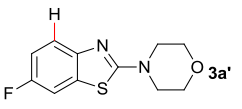
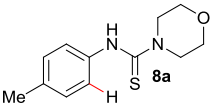
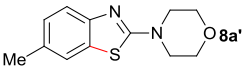
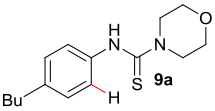
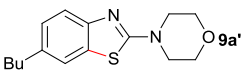
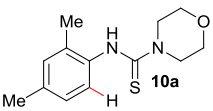
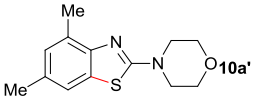


Entry	Substrate	Product	Yield (%)[a]
1			85
2			80
3			68
4			75
5			70
6			75

[a] Yields of pure isolated products after silica gel column chromatography.

Table 3
Cu catalyzed synthesis of 2-aminobenzothiazoles

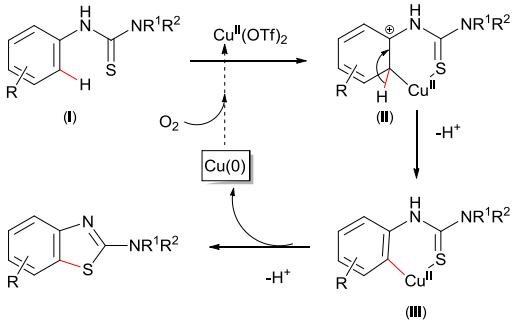


Entry	Substrate	Product	Time (h)/ Yield (%)[a]
1			12/85
2			11/78
3			12/76
4			10/75
5			9/80
6			9.5/85
7			10/84
8			8/81
9			7.5/83
10			6/82

[a] Yields of pure isolated products after silica gel column chromatography.

p-F (**3a**), *p*-Br (**4a**) all provided their corresponding products (**2a′**), (**3a′**) and (**4a′**), respectively. In the case of *o*-halo (−Cl, −F) substituted arylthioureas (**5a**) and (**6a**) both gave benzothiazole (**1a′**) via a dehalogenative path and not by C−H functionalization. Formation of benzothiazole (**1a′**) for substrates (**5a**) and (**6a**) supports our previous observation where a Cu catalyzed reaction prefers dehalogenative C−S bond formation over the C−H activation path. The preferential dehalogenative C−S bond formation over C−H activation was further confirmed with substrate (**7a**) bearing *o*-F group, which gave corresponding benzothiazole (**3a′**) again via a dehalogenative path. Similarly, *N*-arylthioureas possessing electron donating substituents, such as *p*-Me (**8a**), *p*-Bu (**9a**) and 2,4 di-Me (**10a**), on the aryl ring all underwent intramolecular C−S bond formation via C−H functionalization giving their corresponding benzothiazoles (**8a′**), (**9a′**) and (**10a′**), respectively.

During this copper catalyzed intramolecular C−S bond formation protocol it was observed that the presence of electron donating substituents, such as −Me (**8a**), −Bu (**9a**) and 2,4-di-Me (**10a**) in the aromatic scaffolds provided their corresponding benzothiazoles in a shorter reaction time than the substrates bearing electron withdrawing substituents −Cl (**2a**), −F (**3a**) and −Br (**4a**). This observation is consistent with the findings of Nagasawa et al. and others.[13] These results indirectly support the oxidative cyclization mechanism where copper triflate is initially coordinated to the sulfur atom leading to a directed *ortho*-metalation by an electrophilic aromatic substitution path. In the next step formation of a six membered metallacycle is followed by a concomitant reductive elimination to give 2-aminobenzothiazole. The Cu(0) species generated in this step is oxidized to Cu(II) with molecular oxygen thereby maintaining the catalytic cycle (Scheme 2).



Scheme 2. Plausible mechanism for Cu catalyzed oxidative cyclization of *N*-arylthiourea.

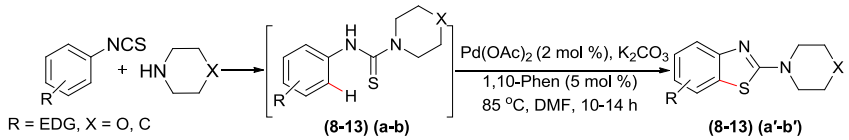
The most notable aspects of the Pd(II) catalyzed C−H activation (C−S bond formation) leading to the synthesis of benzothiazole is, it still prefers C−H activation even in the presence of *o*-halo (−Cl, −F) substituents in thioureas.[6] The above mentioned $Cu(OTf)_2$ catalyzed strategy prefers dehalogenative path even in the presence of less reactive halogens (−Cl, −F) and not the C−H functionalization path. However this Pd-catalyzed method of C−H functionalization was not successful particularly for arylthioureas possessing strongly electron donating groups, such as (−OMe, −OBu). Under the present reaction conditions such thioureas (**12a**) and (**13a**) decomposed to their corresponding amines rather than giving the expected 2-aminobenzothiazoles. Therefore a further tuning of the Pd-catalyst is indeed necessary, which should work both for substrates possessing electron donating as well as electron withdrawing groups.

Ligands are known to assist metals in tuning their reactivity and have been used widely for various Pd-catalyzed C−H functionalizations.[15] Therefore we thought to employ a ligand assisted Pd-catalyzed protocol for arylthioureas possessing electron donating groups in the aromatic rings. Bidentate 1,10-phenanthroline is a well explored ligand in several Pd-catalyzed C−H functionalization reactions,[16] which was chosen for this purpose. Interestingly the substrate *N*-(4-methoxyphenyl)morpholine-4-carbothioamide (**12a**) when reacted in the presence of 5 mol % of $Pd(OAc)_2$ along with 15 mol % of 1,10-phenanthroline and 1 equiv of K_2CO_3 provided the desired product (**12a′**) in 91% isolated yield. With this initial success other ligands, such as L-proline, ethylenediamine, 2,2′-bipyridyl and ethane 1,2-diol were employed for this purpose but all of them gave inferior yields 60%, 5%, 50%, and 35%, respectively, as compared to 1,10-phenanthroline. Other solvents, such as DMSO, 1,4-dioxane, toluene, acetonitrile, and acetone and bases, such as $NaHCO_3$, NaOH, KOH tested were found to be not so effective. Further decreasing the catalyst loading to 2 mol % and ligand loading to 5 mol % the yield remained unchanged (90%). Therefore 2 mol % of $Pd(OAc)_2$ along with 1,10-phenanthroline (5 mol %) in DMF solvent and using K_2CO_3 as the base was found to be the most optimized conditions used for all other substrates bearing electron donating substituents in the aromatic core of arylthioureas.

With the above optimized reaction conditions in hand thioureas (**8a**) and (**8b**) possessing electron donating substituent (*p*-Me) gave corresponding 2-aminobenzothiazoles (**8a′**) and (**8b′**) in excellent yields (Table 4). Similarly *p*-butyl substituted thioureas (**9a**) and (**9b**) were reacted and corresponding 2-aminobenzothiazoles (**9a′**) and (**9b′**) were isolated in good yields. Sterically hindered 2,4 di-Me substituted thioureas (**10a**) and (**10b**) underwent intramolecular C−S bond formation via C−H activation giving 2-aminobenzothiazoles (**10a′**) and (**10b′**), respectively, in excellent yields. 2-Aminobenzothiazoles (**11a′**) and (**11b′**) were obtained regioselectively from their 3,4 di-Me substituted thioureas (**11a**) and (**11b**) as evident from their ^1H NMR. It may be reiterated that the synthesis of 2-aminobenzothiazoles from thioureas were not so successful using Pd(II) catalyzed reaction particularly for substrates possessing strongly electron donating groups.[6,9] However the present ligand assisted Pd(II) catalyzed synthesis was quite successful even for substrate possessing strongly electron donating groups as has been demonstrated for substrates (**12a**), (**12b**), (**13a**), and (**13b**) giving their desired products (**12a′**), (**12b′**), (**13a′**), and (**13b′**) (Table 4) respectively, in excellent yields confirming the active role of ligand in tuning the catalytic activity of Pd(II). The method was however not so successful for substrate possessing electron donating substituent in its *ortho* position as was observed for substrate (**14a**). In the later case the product (**14a′**) was obtained in a mere yield of 45% along with the recovery of starting material (45%) and slight decomposition to its corresponding amine (10%). The failure to obtain product (**14a′**) in good yield could be partly due to the steric hindrance from the *ortho* methoxy group or in achieving the desired transition state for this transformation.

Formation of benzothiazoles from thioureas bearing electron donating groups is possibly going via the mechanism as shown in Scheme 3. Initially the in situ generated Pd−phen complex (**I**), derived from $Pd(OAc)_2$ and 1,10-phenanthroline, is coordinated to sulfur atom of *N*-arylthiourea giving complex (**II**). The complex (**II**) is transformed into a six membered palladacycle giving intermediate complex (**III**). This is then followed by a base-mediated deprotonative metalation with the expulsion of an acetate group giving intermediate (**IV**) as proposed by Inamoto et al.[10b] Subsequent reductive elimination provides 2-aminobenzothiazole with concomitant generation of Pd(0) species (**V**). The in situ generated Pd(0) is further oxidized to Pd(II) by an aerial oxidation, which maintains the catalytic cycle as shown in Scheme 3.

Table 4
Synthesis of 2-aminobenzothiazole from electron donating *N*-arylthioureas



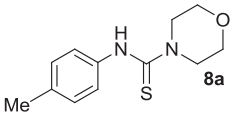
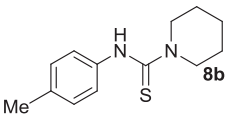
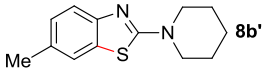
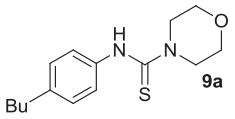
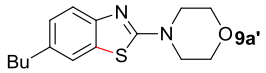
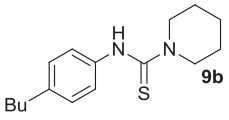
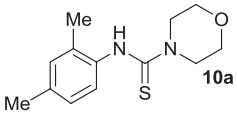
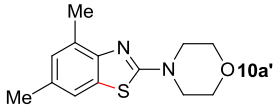
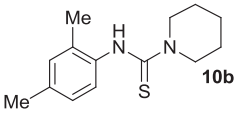
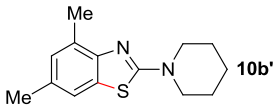
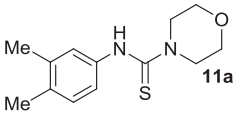
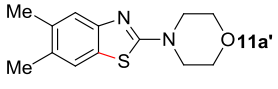
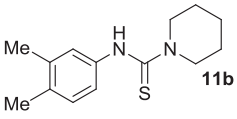
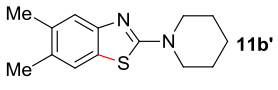
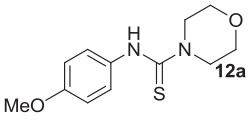
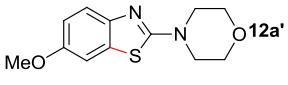
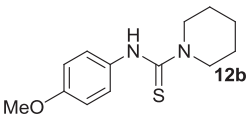
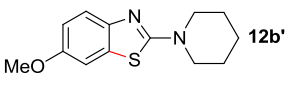
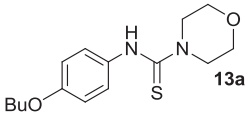
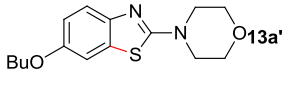
Entry	Substrate	Product	Yield (%)[a]
1			91
2			92
3			91
4			88
5			92
6			91
7			85
8			87
9			90
10			89
11			90

Table 4 (*continued*)

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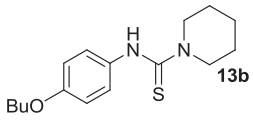
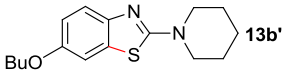
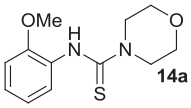
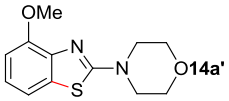
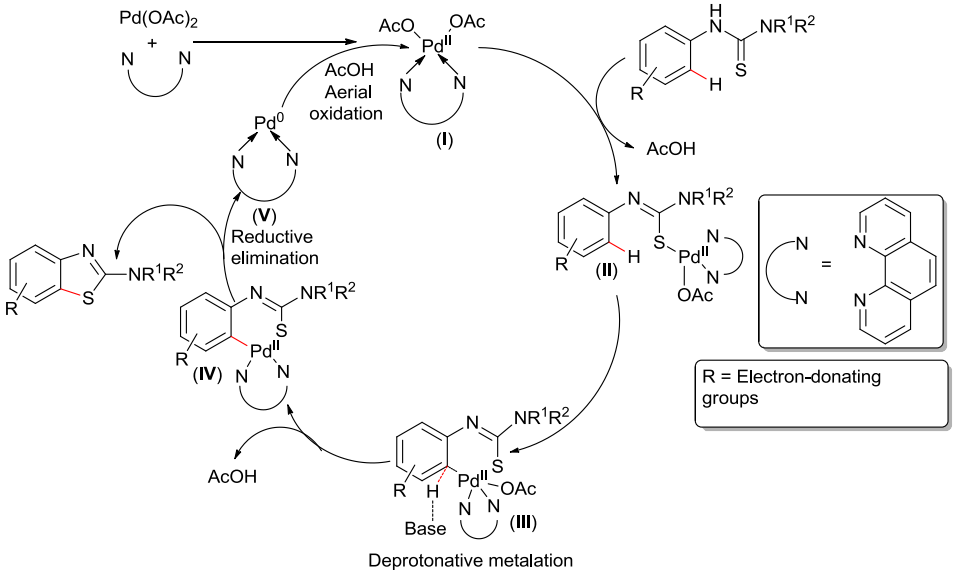
12			89
13			45[b]

[a] Yields of pure isolated products after silica gel column chromatography.
[b] 45% starting material recovered.



Scheme 3. Plausible pathway for ligand assisted Pd-catalyzed synthesis of 2-aminobenzothiazole.

3. Conclusions

In conclusion we have developed two independent strategies for the synthesis of 2-aminobenzothiazoles from thioureas, the first one is via an intramolecular C–H functionalization (C–S bond formation) using environmentally benign Cu-catalyst, $Cu(OTf)_2$. In the second approach a ligand assisted $Pd(OAc)_2$ catalyzed strategy is applied for thioureas possessing electron donating substituents in the aromatic rings. It may be mentioned here that the second strategy is not effective in the absence of ligand. Thus the cheap environmentally acceptable Cu(II) catalyst is as effective as that of a ligand assisted expensive Pd(II) catalyst towards intramolecular C–S bond formation via C–H functionalization.

4. Experimental section

4.1. General remarks

Unless otherwise stated, all reagents were purchased from commercial sources and used without further purification. Reaction progress was monitored by TLC using silica gel 60 F_{254} (0.25 mm) with detection by UV or iodine. Chromatography was performed using silica gel (60–120) mesh size with freshly distilled solvents. Columns were typically packed as slurry and equilibrated with the appropriate solvent system prior to use. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on FT-400 MHz instrument using TMS as an internal standard. Data are presented as follows: chemical shift (parts per million), multiplicity (s=singlet, d=doublet, t=triplet, quin=quintet, m=multiplet, b=broad, br s=broad singlet, br m=broad multiplet), coupling constant *J* (Hertz). Elemental analyses were carried out on an automatic carbon, hydrogen, nitrogen, and sulfur analyser. Melting points were recorded and are uncorrected. IR spectra were recorded in KBr or neat.

4.2. General procedure for preparation of substituted 2-morpholinobenzo[*d*]thiazoles from substituted *N*-(phenyl) morpholine-4-carbothioamide using $Cu(OTf)_2$ (1–10)

Substituted phenyl isothiocyanate (**1**–**10**) (1.5 mmol) was treated with morpholine **a** (1.5 mmol) under neat condition and instant formation of the corresponding thiourea was observed. To this in situ generated thiourea toluene (2 mL) was added and medium was stirred at room temperature for 5 min followed by the addition of copper triflate (10 mol %). After that the reaction mixture was subjected to reflux in a preheated oil bath at 110 °C

under O_2 atmosphere. The progress of the reaction was monitored by TLC. After the completion of the reaction as judged from TLC the reaction mixture was cooled and then admixed with water (1 mL) and the product was extracted with ethyl acetate (2×10 mL). The organic layer was dried over anhydrous sodium sulfate (Na_2SO_4), filtered and evaporated under reduced pressure. The crude products so obtained were further purified through silica gel column chromatograph (hexane/ethyl acetate, 9:1) to yield the pure substituted 2-morpholinobenzo[*d*]thiazole (**1a′**–**10a′**). The identity and purity of the product was further confirmed by spectroscopic analysis. Reaction performed with phenyl isothiocyanate (**1**) (1.5 mmol) and other secondary amines (**b**–**f**) (1.5 mmol) in the above mentioned method and corresponding benzo[*d*]thiazoles (**1b′**–**f′**) were isolated and spectroscopically characterized.

*4.2.1. 4-(Benzo[d]thiazol-2-yl)morpholine (**1a′**).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **1a′** (187 mg, 85%) as white solid; R_f (10% EtOAc/hexane) 0.24; mp 122 °C; ν_{max} (KBr): 2918, 2854, 1591, 1537, 1441, 1377, 1289, 1229, 1113, 1067, 1032, 945, 859, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (dd, 2H, J_1=6.4 Hz, J_2=4.0 Hz, Ar. C–H), 7.27 (t, 1H, J=8.0 Hz, Ar. C–H), 7.07 (t, 1H, J=7.6 Hz, Ar. C–H), 3.80 (t, 4H, J=4.4 Hz, aliphatic–CH_2–), 3.59 (t, 4H, J=4.4 Hz, aliphatic–CH_2–); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 152.5, 130.6, 126.1, 121.7, 120.8, 119.4, 66.2, 48.5; Anal. Calcd for $C_{11}H_{12}N_2OS$: C, 59.97; H, 5.49; N, 12.72; Found C, 60.02; H, 5.55; N, 12.69.

*4.2.2. 2-(Piperidin-1-yl)benzo[d]thiazole (**1b′**).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **1b′** (174 mg, 80%) as white solid; R_f (10% EtOAc/hexane) 0.25; mp 96.5 °C; ν_{max} (KBr): 3063, 2939, 2922, 2848, 1590, 1535, 1440, 1385, 1333, 1287, 1258, 1212, 1121, 1009, 935, 902, 811, 761, 730, 648 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, 2H, J=7.6 Hz, Ar. C–H), 7.25 (t, 1H, J=5.4 Hz, Ar. C–H), 7.02 (t, 1H, J=7.2 Hz, Ar. C–H), 3.55 (s, 4H, aliphatic–CH_2–), 1.63 (s, 6H, aliphatic–CH_2–); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 153.0, 130.7, 125.9, 121.1, 120.6, 118.8, 49.6, 25.3, 24.3; Anal. Calcd for $C_{12}H_{14}N_2S$: C, 66.02; H, 6.46; N, 12.83; found C, 66.08; H, 6.50; N, 12.76.

*4.2.3. 2-(Pyrrolidin-1-yl)benzo[d]thiazole (**1c′**).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **1c′** (138 mg, 68%) as white solid; R_f (10% EtOAc/hexane) 0.22; mp 101 °C; ν_{max} (KBr): 2950, 2868, 1604, 1561, 1544, 1442, 1365, 1341, 1317, 1276, 1258, 1175, 1120, 1069, 859, 747, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, 2H, J=8.4 Hz, Ar. C–H), 7.28 (t, 1H, J=7.6 Hz, Ar. C–H), 7.03 (t, 1H, J=7.6 Hz, Ar. C–H), 3.56 (m, 4H, aliphatic–CH_2–), 2.06 (m, 4H, aliphatic–CH_2–); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 153.4, 130.8, 126.0, 120.8, 120.7, 118.7, 49.6, 25.7; Anal. Calcd for $C_{11}H_{12}N_2S$: C, 64.67; H, 5.92; N, 13.71; found C, 64.71; H, 5.95; N, 13.68.

*4.2.4. 2-(4-Phenylpiperazin-1-yl)benzo[d]thiazole (**1d′**).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **1d′** (221 mg, 75%) as white solid; R_f (10% EtOAc/hexane) 0.24; mp 170 °C; ν_{max} (KBr): 3026, 2861, 1594, 1560, 1539, 1503, 1443, 1384, 1347, 1293, 1249, 1229, 1194, 1158, 1024, 935, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, 2H, J=8.0 Hz, Ar. C–H), 7.33 (m, 3H, Ar. C–H), 7.10 (t, 1H, J=8.0 Hz, Ar. C–H), 6.94 (m, 3H, Ar. C–H), 3.78 (t, 4H, J=5.2 Hz, aliphatic–CH_2–), 3.29 (t, 4H, J=5.2 Hz, aliphatic–CH_2–); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.7, 152.8, 151.0, 130.9, 129.3, 126.2, 121.7, 120.8, 120.7, 119.3, 116.9, 49.1, 48.4; HRMS (ESI) calcd for $C_{17}H_{17}N_3S$ ($M+H^+$) 296.1216, found 296.1214.

*4.2.5. 2-(4-Benzylpiperidin-1-yl)benzo[d]thiazole (**1e′**).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **1e′** (215 mg, 70%) as white solid; R_f (10% EtOAc/hexane) 0.26; mp 114 °C; ν_{max} (KBr): 3061, 3024, 2937, 2920, 2851, 1595, 1539, 1492, 1444, 1388, 1324, 1278, 1258, 1172, 922, 752, 727 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.60 (t, 2H, J=6.4 Hz, Ar. C–H), 7.32 (m, 2H, Ar. C–H), 7.26 (d, 1H, J=7.2 Hz, Ar. C–H), 7.18 (d, 2H, J=8.0 Hz, Ar. C–H), 7.08 (t, 2H, J=8.0 Hz, Ar. C–H), 4.15 (d, 2H, J=13.2 Hz, aliphatic–CH_2–), 3.06 (t, 2H, J=12.8 Hz, aliphatic–CH_2–), 2.59 (d, 2H, J=7.2 Hz, aliphatic–CH_2–), 1.77 (d, 4H, J=10.8 Hz, aliphatic–CH_2–), 1.37 (m, 1H, aliphatic C–H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.7, 153.0, 139.9, 130.8, 129.2, 128.4, 126.2, 126.0, 121.2, 120.7, 118.9, 49.0, 43.0, 38.0, 31.5; HRMS (ESI) calcd for $C_{19}H_{20}N_2S$ ($M+H^+$) 309.0955, found 309.0959.

*4.2.6. 2-Thiomorpholinobenzo[d]thiazole (**1f′**).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **1f′** (187 mg, 75%) as yellow gum; R_f (10% EtOAc/hexane) 0.22; ν_{max} (KBr): 3059, 2936, 2858, 1599, 1531, 1444, 1385, 1359, 1313, 1218, 1054, 1020, 899, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, 1H, J=7.6 Hz, Ar. C–H), 7.52 (d, 1H, J=8.0 Hz, Ar. C–H), 7.28 (t, 1H, J=8.0 Hz, Ar. C–H), 7.06 (t, 1H, J=7.2 Hz, Ar. C–H), 3.93 (t, 4H, J=4.8, aliphatic–CH_2–), 2.71 (t, 4H, J=5.2 Hz, aliphatic–CH_2–); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.2, 152.7, 130.8, 126.2, 121.6, 120.8, 119.2, 51.3, 26.7; Anal. Calcd for $C_{11}H_{12}N_2S_2$: C, 55.90; H, 5.12; N, 11.85; found C, 55.93; H, 5.18; N, 11.79.

*4.2.7. 4-(5-Chlorobenzo[d]thiazol-2-yl)morpholine (**2a′**).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **2a′** (198 mg, 78%) as white solid; R_f (10% EtOAc/hexane) 0.23; mp 108 °C; ν_{max} (KBr): 3051, 2978, 2930, 2902, 2855, 1737, 1587, 1530, 1437, 1375, 1325, 1279, 1234, 1142, 1110, 1070, 1035, 885, 872, 808, 678, 632, 603 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.54 (s, 1H, Ar. C–H), 7.49 (d, 1H, J=8.4 Hz, Ar. C–H), 7.06 (d, 1H, J=2.6 Hz, Ar. C–H), 3.82 (t, 4H, J=5.0 Hz, aliphatic–CH_2–), 3.61 (t, 4H, J=5.0 Hz, aliphatic–CH_2–); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 153.8, 132.1, 129.0, 121.7, 121.5, 119.4, 66.3, 48.5; HRMS (ESI) calcd for $C_{11}H_{11}N_2OClS$ ($M+H^+$) 255.0353, found 255.0350.

*4.2.8. 4-(6-Fluorobenzo[d]thiazol-2-yl)morpholine (**3a′**).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **3a′** (180 mg, 76%) as white solid; R_f (10% EtOAc/hexane) 0.21; mp 145 °C; ν_{max} (KBr): 3058, 2982, 2906, 2883, 2864, 2845, 1903, 1674, 1611, 1539, 1459, 1376, 1343, 1287, 1235, 1181, 1112, 1073, 1029, 948, 920, 844, 805, 710, 651 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.50 (m, 1H, Ar. C–H), 7.31 (d, 1H, J=8 Hz, Ar. C–H), 7.03 (t, 1H, J=9 Hz, Ar. C–H), 3.80–3.82 (m, 4H, aliphatic–CH_2–), 3.57 (t, 4H, J=4.8 Hz, aliphatic–CH_2–); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.7, 159.5, 157.1, 149.0, 131.3, 119.9, 119.8, 114.0, 113.8, 107.7, 107.5, 66.6, 48.5; HRMS (ESI) calcd for $C_{11}H_{11}N_2OFS$ ($M+H^+$) 239.0649, found 239.0651.

*4.2.9. 4-(6-Bromobenzo[d]thiazol-2-yl)morpholine (**4a′**).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **4a′** (222 mg, 75%) as white solid; R_f (10% EtOAc/hexane) 0.25; mp 165–167 °C; ν_{max} (KBr): 2918, 2857, 1591, 1535, 1443, 1372, 1280, 1258, 1229, 1110, 1026, 940, 863, 813 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.68 (s, 1H, Ar. C–H), 7.37 (s, 2H, Ar. C–H), 3.80 (t, 4H, J=4.8 Hz, aliphatic–CH_2–), 3.57 (t, 4H, J=4.8 Hz, aliphatic–CH_2–);

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.1, 151.6, 132.4, 129.4, 123.3, 120.5, 114.0, 66.3, 48.5; Anal. Calcd for $C_{11}H_{11}N_2OSBr$: C, 44.16; H, 3.71; N, 9.36; found C, 44.20; H, 3.72; N, 9.29.

4.3. General procedure for preparation of substituted 2-morpholinobenzo[*d*]thiazole (**8**–**14**) (**a′**–**b′**) from substituted *N*-(phenyl) morpholine-4-carbothioamide (**8**–**14**) using $Pd(OAc)_2$ and 1,10-phenanthroline

Substituted phenyl isothiocyanate (**8**–**14**) (1.5 mmol) was reacted with morpholine **a** (1.5 mmol) under solvent free condition and immediate formation of the corresponding thiourea was observed. To this in situ generated thiourea DMF (2 mL) was added and medium was stirred at room temperature for 5 min followed by the addition of K_2CO_3 (1.5 mmol), 1,10-phenanthroline (5 mol %) and palladium acetate (2 mol %). Then the reaction mixture was subjected to reflux in a preheated oil bath at 85 °C and the progress of the reaction was monitored by TLC. After the completion of the reaction the reaction mixture was admixed with water (1 mL) and the product was extracted with ethyl acetate (2×10 mL). The organic layer was dried over anhydrous sodium sulfate (Na_2SO_4), filtered and evaporated under reduced pressure. The crude product so obtained was further purified through silica gel column chromatograph (hexane/ethyl acetate, 9:1) to yield the pure substituted 2-morpholinobenzo[*d*]thiazole (**8**–**14**) (**a′**–**b′**). The identity and purity of the product was further confirmed by spectroscopic analysis.

*4.3.1. 4-(6-Methylbenzo[d]thiazol-2-yl)morpholine (**8a′**).* Both general procedures were followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **8a′** (189 mg, 81%) (212 mg, 91%) as white solid; R_f (10% EtOAc/hexane) 0.26; mp 135 °C; ν_{max} (KBr): 2963, 2912, 2856, 1599, 1575, 1544, 1464, 1434, 1352, 1281, 1235, 1113, 1026, 943, 811 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, 1H, *J*=8.0 Hz, Ar. C–H), 7.40 (s, 1H, Ar. C–H), 7.09 (d, 1H, *J*=8.0 Hz, Ar. C–H), 3.79 (t, 4H, *J*=4.8 Hz, aliphatic–CH_2–), 3.56 (t, 4H, *J*=4.8 Hz, aliphatic–CH_2–), 2.37 (s, 3H, Ar–CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.6, 150.4, 131.6, 130.7, 127.4, 120.9, 119.0, 66.3, 48.6, 21.3; HRMS (ESI) calcd for $C_{12}H_{14}N_2OS$ ($M+H^+$) 235.09, found 235.09.

*4.3.2. 6-Methyl-2-(piperidin-1-yl)benzo[d]thiazole (**8b′**).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **8b′** (213 mg, 92%) as white solid; R_f (10% EtOAc/hexane) 0.25; mp 106 °C; ν_{max} (KBr): 2942, 2851, 2730, 1604, 1571, 1541, 1463, 1441, 1384, 1358, 1337, 1265, 1243, 1206, 1121, 1009, 810, 626 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, 1H, *J*=8.0 Hz, Ar. C–H), 7.37 (s, 1H, Ar. C–H), 7.07 (d, 1H, *J*=8.4 Hz, Ar. C–H), 3.56 (s, 4H, aliphatic–CH_2–), 2.37 (s, 3H, Ar–CH_3), 1.67 (s, 6H, aliphatic–CH_2–); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.6, 150.9, 130.9, 127.1, 120.8, 118.6, 49.7, 25.4, 24.4, 21.3; HRMS (ESI) calcd for $C_{13}H_{16}N_2S$ ($M+H^+$) 233.1107, found 233.1104.

*4.3.3. 4-(6-Butylbenzo[d]thiazol-2-yl)morpholine (**9a′**).* Both general procedures were followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **9a′** (229 mg, 83%) (251 mg, 91%) as white solid; R_f (10% EtOAc/hexane) 0.28; mp 53 °C; ν_{max} (KBr): 2954, 2921, 2856, 2095, 1731, 1604, 1564, 1536, 1461, 1376, 1340, 1277, 1231, 1111, 1071, 1032, 944, 916, 878, 822, 658 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, 1H, *J*=8.4 Hz, Ar. C–H), 7.42 (s, 1H, Ar. C–H), 7.11–7.13 (m, 1H, Ar. C–H), 3.82 (t, 4H, *J*=4.8 Hz, aliphatic–CH_2–), 3.59 (t, 4H, *J*=5.0 Hz, aliphatic–CH_2–), 2.64 (t, 2H, *J*=7.6 Hz, aliphatic–CH_2–), 1.65–1.54 (m, 2H, aliphatic–CH_2–), 1.40–1.29 (m, 2H, aliphatic–CH_2–), 0.92 (t, 3H, *J*=7.4 Hz, aliphatic–CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.7, 150.6, 136.9, 126.9, 125.7, 120.4, 119.1, 66.4, 48.7, 35.6, 34.1, 22.5, 14.1; HRMS (ESI) calcd for $C_{15}H_{20}N_2OS$ ($M+H^+$) 277.1369, found 277.1370.

*4.3.4. 6-Butyl-2-(piperidin-1-yl)benzo[d]thiazole (**9b′**).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **9b′** (241 mg, 88%) as liquid; R_f (10% EtOAc/hexane) 0.28; ν_{max} (KBr): 2932, 2855, 1602, 1566, 1535, 1463, 1448, 1383, 1354, 1338, 1291, 1261, 1243, 1210, 1200, 1125, 1014, 934, 852, 818, 684 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, 1H, *J*=8.0 Hz, Ar. C–H), 7.38 (s, 1H, Ar. C–H), 7.08 (d, 1H, Ar. C–H), 3.56 (s, 4H, aliphatic–CH_2–), 2.62 (t, 2H, *J*=7.6 Hz, aliphatic–CH_2–), 1.65 (s, 6H, aliphatic–CH_2–), 1.62–1.56 (m, 2H, aliphatic–CH_2–), 1.37–1.26 (m, 3H, aliphatic–CH_3), 0.93–0.86 (m, 2H, aliphatic–CH_2–); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.7, 151.0, 136.2, 130.8, 126.6, 120.2, 118.5, 49.8, 35.6, 34.2, 25.4, 24.4, 22.5, 14.1; HRMS (ESI) calcd for $C_{16}H_{22}N_2S$ ($M+H^+$) 275.1576, found 275.1576.

*4.3.5. 4-(4,6-Dimethylbenzo[d]thiazol-2-yl)morpholine (**10a′**).* Both general procedures were followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **10a′** (203 mg, 82%) (228 mg, 92%) as white solid; R_f (10% EtOAc/hexane) 0.25; mp 116 °C; ν_{max} (KBr): 2956, 2910, 2850, 1580, 1545, 1450, 1376, 1342, 1288, 1233, 1111, 1035, 947, 914, 833 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (s, 1H, Ar. C–H), 6.92 (s, 1H, Ar. C–H), 3.78–3.77 (m, 4H, aliphatic–CH_2–), 3.56–3.55 (m, 4H, aliphatic–CH_2–), 2.52 (s, 3H, Ar–CH_3), 2.34 (s, 3H, Ar–CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 149.6, 131.3, 130.6, 128.9, 128.2, 118.3, 66.4, 48.6, 21.3, 18.3; HRMS (ESI) calcd for $C_{13}H_{16}N_2OS$ ($M+H^+$) 249.1056, found 249.1052.

*4.3.6. 4,6-Dimethyl-2-(piperidin-1-yl)benzo[d]thiazole (**10b′**).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **10b′** (224 mg, 91%) as white solid; R_f (10% EtOAc/hexane) 0.29; mp 100 °C; ν_{max} (KBr): 2989, 2932, 2848, 1727, 1579, 1538, 1462, 1447, 1434, 1384, 1340, 1287, 1266, 1247, 1212, 1122, 1015, 851, 639 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 (s, 1H, Ar. C–H), 6.89 (s, 1H, Ar. C–H), 3.54 (s, 4H, aliphatic–CH_2–), 2.52 (s, 3H, Ar–CH_3), 2.32 (s, 3H, Ar–CH_3), 1.64 (s, 6H, aliphatic–CH_2–); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 149.9, 130.7, 130.5, 128.3, 127.9, 118.2, 49.6, 25.4, 24.5, 21.3, 18.3; HRMS (ESI) calcd for $C_{14}H_{18}N_2S$ ($M+H^+$) 247.1263, found 247.1261.

*4.3.7. 4-(5,6-Dimethylbenzo[d]thiazol-2-yl)morpholine (**11a′**).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **11a′** (211 mg, 85%) as white solid; R_f (10% EtOAc/hexane) 0.24; mp 131 °C; ν_{max} (KBr): 2966, 2921, 2856, 1607, 1531, 1444, 1375, 1342, 1283, 1262, 1227, 1114, 1069, 1021, 899, 858, 800 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (s, 2H, Ar. C–H), 3.83 (t, 4H, *J*=4.8 Hz, aliphatic–CH_2–), 3.59 (t, 4H, *J*=4.8 Hz, aliphatic–CH_2–), 2.31 (s, 3H, Ar–CH_3), 2.29 (s, 3H, Ar–CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 151.1, 135.1, 130.8, 128.0, 121.3, 120.3, 66.5, 48.7, 20.3, 19.9; HRMS (ESI) calcd for $C_{13}H_{16}N_2OS$ ($M+H^+$) 249.1056, found 249.1059.

*4.3.8. 5,6-Dimethyl-2-(piperidin-1-yl)benzo[d]thiazole (**11b′**).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **11b′** (214 mg, 87%) as white solid; R_f (10% EtOAc/hexane) 0.26; mp 120 °C; ν_{max} (KBr): 2935, 2853, 1611, 1536, 1444, 1337, 1285, 1248, 1215, 1122, 1008, 989, 864, 796, 683, 635, 608 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (s, 1H, Ar. C–H), 7.32 (s, 1H, Ar. C–H), 3.55 (s, 4H, aliphatic–CH_2–), 2.28 (s, 6H, Ar–CH_3), 1.66 (s, 6H,

aliphatic–CH_2–); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.8, 151.5, 134.7, 130.0, 128.0, 121.1, 119.8, 49.8, 25.5, 24.5, 20.3, 19.9; HRMS (ESI) calcd for $C_{14}H_{18}N_2S$ ($M+H^+$) 247.1263, found 247.1262.

*4.3.9. 4-(6-Methoxybenzo[d]thiazol-2-yl)morpholine (**12a**′).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **12a**′ (225 mg, 90%) as white solid; R_f (10% EtOAc/hexane) 0.17; mp 134 °C; ν_{max} (KBr): 3065, 2945, 2849, 1600, 1576, 1548, 1475, 1440, 1376, 1341, 1265, 1235, 1182, 1112, 1072, 1058, 1026, 952, 914, 835, 811, 652 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, 1H, J=8.8 Hz, Ar. C–H), 7.15 (s, 1H, Ar. C–H), 6.91 (d, 1H, J=8.8 Hz, Ar. C–H), 3.81 (s, 7H, Ar–OCH_3+aliphatic–CH_2–), 3.56 (t, 4H, J=4.8 Hz, aliphatic–CH_2–); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 155.4, 146.8, 131.7, 119.9, 113.9, 105.4, 66.4, 56.0, 48.7; HRMS (ESI) calcd for $C_{12}H_{14}N_2O_2S$ ($M+H^+$) 251.0849, found 251.0845.

*4.3.10. 6-Methoxy-2-(piperidin-1-yl) benzo[d]thiazole (**12b**′).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **12b**′ (220 mg, 89%) as white solid; R_f (10% EtOAc/hexane) 0.18; mp 72 °C; ν_{max} (KBr): 3054, 2935, 2854, 1599, 1566, 1533, 1461, 1448, 1381, 1363, 1333, 1251, 1221, 1123, 1026, 952, 914, 835, 811, 652 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, 1H, J=8.8 Hz, Ar. C–H), 7.13 (s, 1H, Ar. C–H), 6.88 (d, 1H, J=2.8 Hz, Ar. C–H), 3.80 (s, 3H, Ar–OCH_3), 3.54 (s, 4H, aliphatic–CH_2–), 1.67 (s, 6H, aliphatic–CH_2–); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.9, 155.0, 147.3, 131.8, 119.4, 113.6, 105.5, 56.1, 49.8, 25.5, 24.5; HRMS (ESI) calcd for $C_{13}H_{16}N_2OS$ ($M+H^+$) 249.1056, found 249.1053.

*4.3.11. 4-(6-Butoxybenzo[d]thiazol-2-yl)morpholine (**13a**′).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **13a**′ (263 mg, 90%) as white solid; R_f (10% EtOAc/hexane) 0.19; mp 85 °C; ν_{max} (KBr): 2965, 2939, 2876, 2843, 1596, 1567, 1537, 1462, 1451, 1398, 1371, 1338, 1326, 1286, 1260, 1227, 1179, 1112, 1060, 1040, 1007, 946, 922, 854, 826, 812, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, 1H, J=8.8 Hz, Ar. C–H), 7.14 (s, 1H, Ar. C–H), 6.90 (d, 1H, J=2.8, Ar. C–H), 3.94 (t, 2H, J=6.6 Hz, Ar–OCH_2–), 3.80 (t, 4H, J=4.8 Hz, aliphatic–CH_2–), 3.54 (t, 4H, J=5.0 Hz, aliphatic–CH_2–), 1.78–1.72 (m, 2H, aliphatic–CH_2–), 1.53–1.44 (m, 2H, aliphatic–CH_2–), 0.99–0.95 (t, 3H, J=7.4 Hz, aliphatic–CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 154.8, 146.6, 131.6, 119.8, 114.4, 106.0, 68.5, 66.3, 48.6, 31.5, 19.3, 14.0; HRMS (ESI) calcd for $C_{15}H_{22}N_2O_2S$ ($M+H^+$) 293.1318, found 293.1320.

*4.3.12. 6-Butoxy-2-(piperidin-1-yl) benzo[d]thiazole (**13b**′).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **13b**′ (258 mg, 89%) as white solid; R_f (10% EtOAc/hexane) 0.20; mp 68 °C; ν_{max} (KBr): 3079, 2928, 2858, 1722, 1606, 1540, 1462, 1449, 1368, 1338, 1285, 1246, 1209, 1124, 1058, 1013, 933, 860, 799, 642 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, 1H, J=8.8, Ar. C–H), 7.12 (s, 1H, Ar. C–H), 6.87 (d, 1H, J=2.6 Hz, Ar. C–H), 3.93 (t, 2H, J=6.4 Hz, Ar–OCH_2–), 3.52 (s, 4H, aliphatic–CH_2–), 1.71–1.76 (m, 2H, aliphatic–CH_2–), 1.65 (s, 6H, aliphatic–CH_2–), 1.45–1.51 (m, 2H, aliphatic–CH_2–), 0.97 (t, 3H, J=7.4 Hz, aliphatic–CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 154.4, 147.1, 131.7, 119.3, 114.2, 106.1, 68.6, 49.7, 31.6, 25.4, 24.4, 19.4, 14.0; HRMS (ESI) calcd for $C_{16}H_{22}N_2OS$ ($M+H^+$) 291.0849, found 291.0846.

*4.3.13. 4-(4-Methoxybenzo[d]thiazol-2-yl)morpholine (**14a**′).* The general procedure was followed. The product was purified by column chromatography (10% EtOAc/hexane) to give the title compound **14a**′ (112 mg, 45%) as white solid; R_f (10% EtOAc/hexane) 0.11; mp 134 °C; ν_{max} (KBr): 3065, 2934, 2856, 1739, 1595, 1544, 1477, 1440, 1421, 1378, 1326, 1289, 1268, 1227, 1182, 1113, 1045, 943, 915, 861, 762, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.23 (d, 1H, J=8.0 Hz, Ar. C–H), 7.06 (t, 1H, J=8.0 Hz, Ar. C–H), 6.82 (d, 1H, J=8.0 Hz, Ar. C–H), 3.97 (s, 3H, Ar–OCH_3), 3.81 (t, 4H, J=5.0 Hz, aliphatic–CH_2–), 3.63 (t, 4H, J=4.8 Hz, aliphatic–CH_2–); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4, 150.8, 142.0, 131.7, 122.4, 113.3, 107.3, 66.4, 55.9, 48.6; HRMS (ESI) calcd for $C_{12}H_{14}N_2O_2S$ ($M+H^+$) 251.0849, found 251.0850.

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Supplementary data

Copies of ^1H and ^{13}C NMR and HRMS spectra of products are available. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.08.025.

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