Concise Report

copper, sulfur heterocycles, oxidation, cyclization

CJC Chinese Journal of Chemistry 中国化学 · An International Journal

Copper-Catalyzed Benzylic C—H Functionalization, Oxidation and Cyclization of Methylarenes: Direct Access to 2-Arylbenzothiazoles†

Wentao Yu, Wanqing Wu, and Huanfeng Jiang*

Key Lab of Functional Molecular Engineering of Guangdong Province, School of Chemistry and Chemical Engineering, South China University of Technology, Guangzhou, Guangdong 510640, China

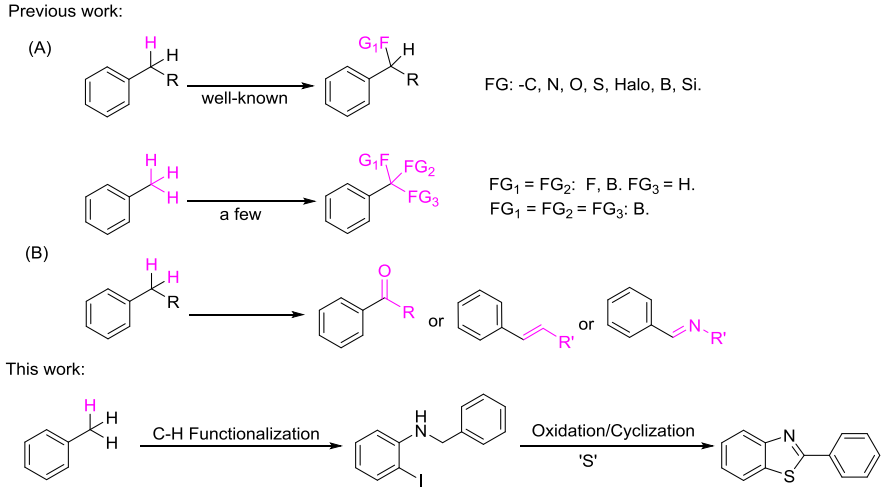
Cite this paper: *Chin. J. Chem.* **2019**, *37*, 1158—1166. **DOI: 10.1002/cjoc.201900340**

Summary of main observation and conclusion The direct C—H functionalization of methylarenes is of great significance. Herein, a copper-catalyzed oxidative C—N/C—S bond formation through benzylic C(sp^3)—H functionalization, oxidation and cyclization of methylarenes is reported. Various 2-arylbenzothiazoles have been synthesized in moderate to excellent yields with readily available *o*-iodoaniline, potassium sulfide, and methylarenes as raw materials.

Background and Originality Content

As an inexpensive, fundamental and important feedstock for the petrochemical industry, methylarenes have long been regarded as one of the most widely used raw materials for a great variety of organic transformations. Therefore, the selective benzylic C(sp^3)—H functionalization is particularly important, which provides a strategic means to utilize this resource. Recent research in benzylic C(sp^3)—H functionalization has mostly focused on mono C(sp^3)—H functionalization for the construction of C—C,[1] C—N,[2] C—O,[3] C—halo,[4] C—B,[5] and C—Si[6] single bonds, which has become a powerful method in synthetic chemistry (Scheme 1A). On the other hand, only a few examples have been reported through double/triple C(sp^3)—H functionalization of benzylic C(sp^3)—H bonds to construct C—F/C—B bonds by Chen,[7] Tang,[8] Baxter,[9] and Chirik,[10] *et al.* (Scheme 1A). In addition, a series of elegant methods were successfully applied to construct C=O, C=C, and C=N double bonds (Scheme 1B). The direct oxidation of benzylic C(sp^3)—H bond to aryl ketone was the most common.[11-16] In 2012, Zhang[17] and Patel[18] accomplished a Pd-catalyzed benzylic C(sp^3)—H arylation/oxidation reaction. Later, Li[19] developed a potassium iodide-catalyzed three-component synthesis of quinazolines *via* benzaldehyde intermediate. Hiyama[20] and Matsuzaka[21] reported a direct dehydrative condensation of benzylic C—H bonds. A practical Brønsted acid promoted-benzylic C—H functionalization of 2-alkylazaarenes and nucleophilic addition to nitroso compounds was also developed by Yang.[22] Punniyamurthy developed a copper(II)-catalyzed tandem cross-coupling of methylarenes with anilines followed by $TMSN_3$ *via* triple C—N bond formation.[23] To date, constructing C—N/C—S bonds through C(sp^3)—H functionalization of methylarenes, to the best of our knowledge, has not been reported. In addition, the selective oxidative C(sp^3)—H amination of methylarenes still suffered from some limitations. Oxidative state amine, amide and aniline bearing strong electron-withdrawing groups were mostly applied to this transformation. On the contrary, simple anilines and electron-rich anilines could be hard to transform to the desired products since they were easy to suffer from oxidation or homodimerization.[23] On the other hand, only a few examples of building C(sp^3)—S bonds were reported by Lei,[24] Qing,[25] Wu,[26] and Bolm.[27]

Scheme 1 C—H Functionalization of Methylarenes



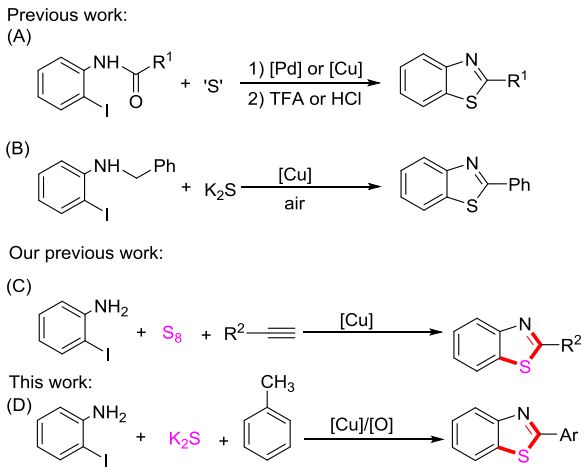
*E-mail: jianghf@scut.edu.cn

† Dedicated to the 30th Anniversary of State Key Laboratory of Organometallic Chemistry.

For submission: https://mc.manuscriptcentral.com/cjoc
For articles: https://onlinelibrary.wiley.com/journal/16147065

Aryl-substituted benzothiazoles, especially for 2-arylbenzothiazoles, are one of the most important heterocycles, which have been extensively investigated for applications in bioactive natural compounds, important drugs and advanced functional materials (Scheme 2).[28] Previous studies for the synthesis of 2-arylbenzothiazoles mainly focused on: (i) condensation of 2-aminobenzenethiols with aldehydes, ketones, alcohols, carboxylic acids, or nitriles;[29] (ii) direct arylation of benzothiazoles[30] or (iii) intramolecular cyclization of thiobenzanilides,[31] and (iiii) three-component annulations.[32] Itoh,[33] Ma,[34] Sekar,[35] Liang,[36] and Lee[37] *et al.* developed an efficient synthesis of benzothiazoles using 2-haloanilides and thiol surrogates *via* palladium- or copper-catalyzed double C—N/C—S bond formation (Schemes 2A and 2B). We have also developed an efficient protocol for the synthesis of benzothiazoles by C≡C triple bond cleavage of the alkyne moiety (Scheme 2C).[38] Noteworthily, Wei reported a simple synthetic strategy with methylaromatics, aniline, and elemental sulfur at 275 °C.[32f] Deng has developed a novel oxidative approach for the synthesis of 2-arylbenzothiazoles from aromatic amines, benzaldehydes, and elemental sulfur.[32b] Inspired by these works, we speculated that direct transformation of methylarenes *via* C—H functionalization of benzylic C(sp^3)—H bonds under Cu/[O] catalytic system should provide an atom- and step-economic strategy to construct benzothiazole products. Herein, we report a copper-catalyzed oxidative annulation through benzylic C(sp^3)—H of methylarenes with 2-iodoaniline and potassium sulfide (Scheme 2D).

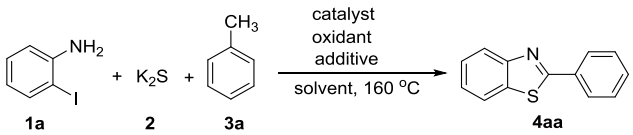
Scheme 2 Methylarenes methods for the synthesis of benzothiazole



Results and Discussion

Our work was initiated with the reaction of 2-iodoaniline (**1a**), potassium sulfide (**2**) and toluene (**3a**) in the presence of CuI and DTBP (Table 1, entry 1). After 12 h, although only a slight of the desired product **4aa** was detected by using toluene as the sole solvent, we were pleased to find that the direct C(sp^3)—H amination of toluene was afforded. Then, a series of mixed solvents were tested, which revealed that DMSO was the most efficient (entries 2—5). Next, examination of various copper salts revealed that $CuCl_2$ was the most suitable catalyst, which could improve the reaction efficiency (entries 6—9). Further evaluation of oxidants, such as TBHP, DDQ, and H_2O_2, indicated DTBP was the best choice (entries 10—12). Different additives were also investigated, and the product was formed in 82% yield in the presence of Li_2CO_3 and H_2O (entries 13—18). Control experiments revealed that copper was beneficial to this transformation (entry 19). Reaction temperature, raw ration, and more detailed investigation on the yields were displaced in Supporting Information (Table S1).

Table 1 Optimization of reaction conditions[a]



1a **2** **3a** **4aa**

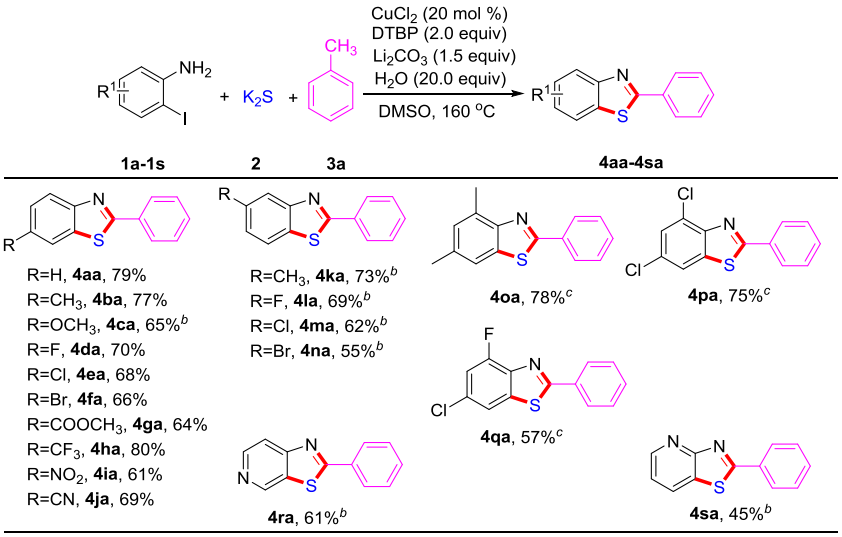
Entry	Catalyst	Oxidant	Additive	Solvent	Yield[b]/%
1	CuI	DTBP	—	—	Trace
2	CuI	DTBP	—	DMF	35
3	CuI	DTBP	—	DMSO	61
4	CuI	DTBP	—	MeCN	NR
5	CuI	DTBP	—	DCE	NR
6	$CuBr_2$	DTBP	—	DMSO	50
7	$CuCl_2$	DTBP	—	DMSO	66
8	CuBr	DTBP	—	DMSO	30
9	$Cu(OTf)_2$	DTBP	—	DMSO	57
10	$CuCl_2$	TBHP	—	DMSO	48
11	$CuCl_2$	DDQ	—	DMSO	44
12	$CuCl_2$	H_2O_2	—	DMSO	32
13	$CuCl_2$	DTBP	Li_2CO_3	DMSO	75
14	$CuCl_2$	DTBP	LiBr	DMSO	66
15	$CuCl_2$	DTBP	K_2CO_3	DMSO	33
16	$CuCl_2$	DTBP	*t*BuOLi	DMSO	18
17	$CuCl_2$	DTBP	DABCO	DMSO	35
18[c]	**$CuCl_2$**	**DTBP**	**Li_2CO_3/H_2O**	**DMSO**	**82 (79)**
19[c]	—	DTBP	Li_2CO_3/H_2O	DMSO	8

[a] Reaction conditions: **1a** (0.20 mmol), **2** (0.60 mmol), **3a** (2 mL), catalyst (0.04 mmol), oxidant (0.40 mmol) and additive (0.30 mmol) for 12 h in the indicated solvent (1.0 mL). [b] Determined by GC-MS using dodecane as the internal standard. The value in parentheses is the isolated yield. [c] 20.0 equiv of H_2O. DTBP = di-*tert*-butyl peroxide. TBHP = *tert*-butyl hydroperoxide. DDQ = 2,3-dicyano-5,6-dichlorobenzoquinone. DABCO = 1,4-diazabicyclo[2.2.2]octane.

With the optimal reaction conditions in hand, the scope for the synthesis of 2-substituted benzothiazoles **4** was then investigated, and the results are summarized in Table 2. The study of the substituent effect on the aryl rings of the 2-iodoaniline derivatives showed that both electron-donating groups, such as 4-methyl, 4-methoxy, 5-methoxy (**4ba**, **4ca**, **4ka**), and electron-withdrawing groups, such as halo, $COOCH_3$, CF_3, NO_2, and CN (**4da—4ja, 4la—4na**) were all compatible with this catalytic system and transformed to the desired products in moderate to excellent yields. Meanwhile, the reactions of the 2-iodoaniline substrates bearing two substituents gave the desired products (**4oa—4qa**) in good yields. Other variants such as 3-iodopyridin-4-amine and 3-iodopyridin-2-amine could also provide the expected products in 61% and 45% yields, respectively (**4ra**, **4sa**).

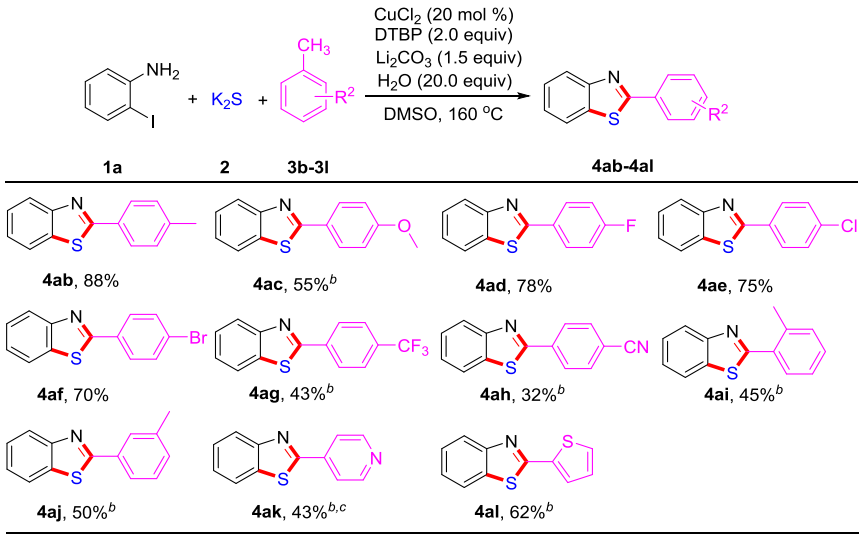
To further examine the scope and limitations of the reaction, various toluene analogues were tested as the substrates for the reaction. As shown in Table 3, the reaction of *p*-xylene with 2-iodoaniline afforded 88% yield of the desired product (**4ab**). The substrates **3** possessing halo group, such as fluoro, chrolo and bromine, could be transformed smoothly and obtained the products in good yields (**4ad—4af**). However, the toluene bearing strong electron-donating/withdrawing groups, such as OCH_3, CF_3, CN, at the phenyl ring only gave moderate yields (**4ac**, **4ag**, **4ah**). Then, the steric hindrance effects in aromatics were examined.

Table 2 Scope of *o*-Iodoanilines[a]



[a] Reaction conditions: **1** (0.20 mmol), **2** (0.60 mmol), **3** (2 mL), $CuCl_2$ (0.04 mmol), DTBP (0.40 mmol) Li_2CO_3 (0.30 mmol) and H_2O (4 mmol) in 1.0 mL of DMSO at 160 °C for 12h. [b] Without H_2O. [c] 24 h.

Table 3 Scope of methylarenes[a]



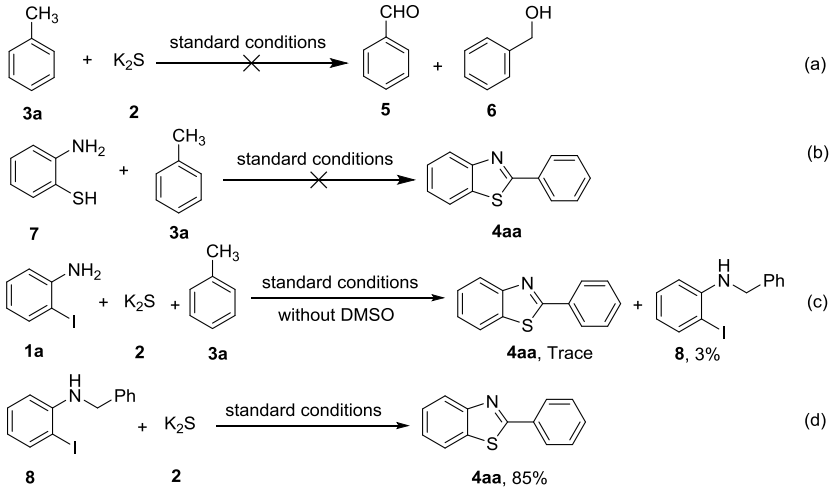
[a] Reaction conditions: **1a** (0.20 mmol), **2** (0.60 mmol), **3** (2 mL), $CuCl_2$ (0.04 mmol), DTBP (0.40 mmol) Li_2CO_3 (0.30 mmol) and H_2O (4 mmol) in 1.0 mL of DMSO at 160 °C for 12h. [b] **3** (1 mL). [c] 24 h.

The reaction of *o*-xylene (**4ai**) and *m*-xylene (**4aj**) gave the desired products in moderate yields. These results indicated the steric and electronic effects affected the product formation. 4-Methylpyridine and 2-methylthiophene were also tolerated in the reaction, and the desired products **4ak** and **4al** were isolated in the yields of 43% and 62%, respectively.

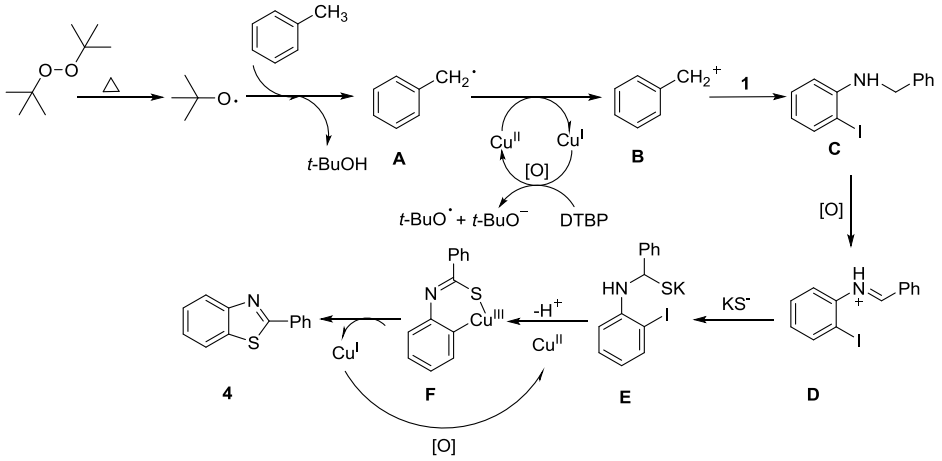
To gain more insights into the mechanism of this transformation, a series of control experiments were then performed (Scheme 3). Without 2-iodoaniline **1a**, the treatment of toluene **3a** and potassium sulfide **2** under the standard conditions could not afford the benzaldehyde **5** and benzyl alcohol **6** (Scheme 3a). Furthermore, no product was observed using 2-aminothiophenol **7** instead of 2-iodoaniline **1a** and potassium sulfide **2** (Scheme 3d). These results indicated that benzaldehyde, benzyl alcohol or 2-aminothiophenol should not be the intermediate of this process. When the reaction was conducted with toluene as the sole solvent, the C(sp^3)—H adjacent to nitrogen product **8** was detected. Moreover, the product **8** was then smoothly transferred into the final benzothiazole under the standard conditions (Schemes 3e and 3f). Therefore, we speculated that the *N*-benzyl-2-iodoaniline **8** might be a key intermediate.

Based on these observations, a tentative mechanism for the product formation is proposed in Scheme 4. Initially, the *tert*-butoxyl radical is generated from DTBP.[39] Then, the *tert*-butoxyl radical abstracts the hydrogen atom of toluene to afford benzyl radical **A**.[39] A single-electron transfer (SET) from **A** to copper(II) leads to cation **B** and copper(I), which can be oxidized to copper(II) for catalytic recycle by DTBP.[24,40] Next, the nucleophilic reaction of amine **1** with the benzyl cation **B** forms products **C** and **D**.[2a] Subsequently, **E** is formed *via* an intermolecular nucleophilic attack with K_2S.[32d,41] Next, oxidative addition and ligand exchange with Cu^{II} species produce a putative Cu^{III} intermediate **F**.[42] Finally, reductive elimination affords the desired product. Meanwhile, the Cu^{I} can be oxidized to regenerate the Cu^{II} species.

Scheme 3 Control experiments



Scheme 4 Proposed mechanism



Conclusions

In summary, we have developed a novel Cu-catalyzed oxidative annulation of *o*-iodoanilines, potassium sulfide and methylarenes. Through this method, benzylic C(sp^3)—H bonds of methylarenes were transferred into C—N/C—S bonds. This method tolerated a wide range of functional groups and provided an effective approach to synthesize 2-arylbenzothiazoles. Mechanistic studies revealed that C(sp^3)—H amination of methylarenes should be a key path.

Experimental

General information

Unless otherwise stated, all reagents and solvents were purchased from commercial suppliers and used without further purification. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 MHz NMR spectrometer using $CDCl_3$ as solvent and TMS as an internal standard. IR spectra were obtained with an infrared spectrometer on either potassium bromide pellets or liquid films between two potassium bromide pellets. GC–MS data were obtained using electron ionization. HRMS was carried out on a high-resolution mass spectrometer (LCMS-IT-TOF). Melting points were measured using a melting point instrument and were uncorrected.

General procedure for the synthesis of benzo[*d*]thiazole products 4

A 25 mL dried Schlenk tube was added the mixture of 2-iodoaniline **1a** (0.20 mmol), K_2S **2** (0.60 mmol), toluene **3a** (2.0 mL), CuI (0.04 mmol), Li_2CO_3 (0.30 mmol), DTBP (0.4 mmol) and H_2O (4 mmol) in DMSO (1.0 mL) successively. The reaction was then allowed to stir at 160 °C for 12 h. Upon completion, the reaction mixture was washed by saturated NaCl aqueous solution (2×10 mL) and then extracted with ethyl acetate (2×10 mL), and the organic layers were combined, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was separated by column chromatography (petroleum ether/ethyl acetate 10 : 1—50 : 1) to give the pure products.

2-Phenylbenzo[4,5]thieno[3,2-*d*]thiazole (3aa).[38] White solid; mp 134—136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.29 (d, J = 8.0 Hz, 1H), 8.06 (d, J = 6.8 Hz, 2H), 7.84 (d, J = 8.0 Hz, 1H), 7.61—7.36 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 170.6, 156.2, 142.8, 134.1, 130.9, 130.6, 130.3, 129.1, 126.6, 125.1, 125.1, 123.3, 121.9; IR (KBr) ν_{max}: 3046, 2918, 1464, 1266, 1223, 748, 669 cm^{-1}; HRMS (ESI): calcd for $C_{15}H_{10}NS_2$ $[M+H]^+$: 268.0249, found: 268.0250.

2-Phenylbenzo[*d*]thiazole (4aa).[38] White solid (33 mg, 79%); mp 113—114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.12—8.05 (m, 3H), 7.91 (d, J = 7.8 Hz, 1H), 7.70—7.50 (m, 4H), 7.41—7.31 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.1, 154.0, 135.0, 133.6, 131.0,

129.0, 127.6, 126.3, 125.2, 123.2, 121.6. IR (KBr) ν_{max}: 3015, 1661, 1455 964, 798, 677 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 211 $[M]^+$, 184, 167, 108, 82, 69.

6-Methyl-2-phenylbenzo[*d*]thiazole (4ba).[38] White solid (35 mg, 77 %); mp 125—126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.08 (dd, *J* = 6.6, 2.7 Hz, 2H), 7.96 (d, *J* = 8.3 Hz, 1H), 7.69 (s, 1H), 7.51—7.45 (m, 3H), 7.30 (d, *J* = 8.3 Hz, 1H), 2.50 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 167.0, 152.3, 135.3, 135.2, 133.8, 130.7, 128.9, 127.9, 127.4, 122.7, 121.3, 21.5. IR (KBr) ν_{max}: 2992, 2888, 1662, 1558, 1456, 961, 758, 677 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 225 $[M]^+$, 209, 180, 148, 121, 112, 77.

6-Methoxy-2-phenylbenzo[*d*]thiazole (4ca).[38] White solid (31 mg, 65%); mp 116—117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.07—8.00 (m, 2H), 7.96 (d, *J* = 8.9 Hz, 1H), 7.50—7.43 (m, 3H), 7.34 (d, *J* = 2.0 Hz, 1H), 7.10—7.08 (m, 1H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 165.5, 157.8, 148.6, 136.4, 133.7, 130.5, 128.9, 127.2, 123.7, 115,6, 104.1, 55.7. IR (KBr) ν_{max}: 3035, 1423, 1244, 959, 844, 763, 677 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 241 $[M]^+$, 226, 198, 171, 120, 95, 77.

6-Fluro-2-phenylbenzo[*d*]thiazole (4da).[38] White solid (32 mg, 70%); mp 134—135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.06 (m, 2H), 8.01 (m, 1H), 7.58 (m, 1H), 7.55—7.43 (m, 3H), 7.26—7.19 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 167.8, 160.5 (d, *J* = 244 Hz), 150.8, 136.0 (d, *J* = 11 Hz), 133.4, 131.0, 129.0, 127.4, 124.1 (d, *J* = 10 Hz), 114.9 (d, *J* = 24Hz), 107.8 (d, *J* = 26 Hz); IR (KBr) ν_{max}: 1661, 1468, 1290, 956, 832, 674 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 229 $[M]^+$, 202, 185, 152, 126, 101, 82, 69.

6-Chloro-2-phenylbenzo[*d*]thiazole (4ea).[29d] White solid (33 mg, 68%); mp 150—151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.08—8.06 (m, 2H), 7.98 (d, *J* = 8.7 Hz, 1H), 7.87 (d, *J* = 1.6 Hz, 1H), 7.54—7.47 (m, 3H), 7.46—7.44 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 168.5, 152.7, 136.2, 133.2, 131.2, 131.1, 129.1, 127.5, 127.1, 123.9, 121.2; IR (KBr) ν_{max}: 3069, 1650, 1472, 1288, 959, 825, 756, 674 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 245 $[M]^+$, 218, 209, 142, 107, 69.

6-Bromo-2-phenylbenzo[*d*]thiazole (4fa).[38] White solid (38 mg, 66%); mp 157—158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.07—8.05 (m, 2H), 8.00 (d, *J* = 1.7 Hz, 1H), 7.90 (d, *J* = 8.7 Hz, 1H), 7.59—7.56 (m, 1H), 7.50—7.48 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 168.5, 153.0, 136.6, 133.1, 131.2, 129.8, 129.1, 127.5, 124.3, 124.1, 118.7; IR (KBr) ν_{max}: 3064, 1650, 1473, 1298, 1230, 959, 820, 753, 676 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 289 $[M]^+$, 210, 188, 144, 107, 77, 69.

Methyl 2-phenylbenzo[*d*]thiazole-6-carboxylate (4ga).[31d] White solid (34 mg, 64%); mp 159—160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.62 (s, 1H), 8.19—8.07 (m, 4H), 7.51 (d, *J* = 5.5 Hz, 3H), 3.97 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 171.5, 166.6, 157.0, 134.9, 133.1, 131.6, 129.1, 127.7, 127.5, 126.9, 123.8, 122.8, 52.3; IR (KBr) ν_{max}: 3216, 1708, 1453, 1271, 1109, 965, 759 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 269 $[M]^+$, 238, 210, 183, 166, 108, 63.

2-Phenyl-6-(trifluoromethyl)benzo[*d*]thiazole (4ha).[38] Yellow solid (45 mg, 80%); mp 160—161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.17 (s, 1H), 8.13 (d, *J* = 8.6 Hz, 1H), 8.11—8.04 (m, 2H), 7.72 (d, *J* = 8.6 Hz, 1H), 7.56—7.45 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 171.0, 156.0, 135.0, 132.9, 131.6, 129.1, 127.7, 142.2 (q, *J* = 32 Hz), 124.2 (q, *J* = 271 Hz), 123.4, 123.2 (q, *J* = 3 Hz), 119.2 (q, *J* = 4 Hz); IR (KBr) ν_{max}: 2890, 1663, 1474, 1307, 1111, 962, 838, 756, 677 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 279 $[M]^+$, 260, 210, 176, 157, 132, 77, 69.

6-Nitro-2-phenylbenzo[*d*]thiazole (4ia).[31d] Yellow solid (31 mg, 61%); mp 191—193 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.82 (s, 1H), 8.36 (d, *J* = 9.0 Hz, 1H), 8.13—8.10 (m, 3H), 7.59—7.51 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 173.7, 157.8, 144.9, 135.3, 132.7, 132.2, 129.3, 127.9, 123.3, 121,9, 118.2; IR (KBr) ν_{max}: 2997, 1655, 1514, 1328, 956, 843, 755, 676 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 256 $[M]^+$, 226, 210, 198, 183, 139, 107, 95, 77.

2-Phenylbenzo[*d*]thiazole-6-carbonitrile (4ja).[31d] Yellow solid (32 mg, 69%); mp 197—198 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.22 (s, 1H), 8.12—8.09 (m, 3H), 7.72 (d, *J* = 8.5 Hz, 1H), 7.58—7.48 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 172.2, 156.4, 135.4, 132.6, 132.0, 129.5, 129.2, 127.8, 126.3, 123.8, 118.7, 108.5; IR (KBr) ν_{max}: 2923, 2228, 1647, 1463, 1260, 965, 831, 755, 675 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 236 $[M]^+$, 209, 164, 133, 104, 82, 69.

5-Methyl-2-phenylbenzo[*d*]thiazole (4ka).[38] White solid (33 mg, 73%); mp 145—146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.13—8.04 (m, 2H), 7.89 (s, 1H), 7.77 (d, *J* = 8.2 Hz, 1H), 7.53—7.46 (m, 3H), 7.22 (d, *J* = 8.2 Hz, 1H), 2.52 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 168.2, 154.5, 136.4, 133.7, 132.0, 130.8, 129.0, 127.5, 126.8, 123.2, 121.1, 21.5; IR (KBr) ν_{max}: 3058, 1658, 1454, 1250, 954, 762, 683 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 225 $[M]^+$, 209, 193, 165, 121, 112, 77.

5-Fluoro-2-phenylbenzo[*d*]thiazole (4la).[32a] White solid (32 mg, 69%); mp 111—112 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.08 (dd, *J* = 6.5, 2.8 Hz, 2H), 7.82 (dd, *J* = 8.8, 5.1 Hz, 1H), 7.75 (dd, *J* = 9.5, 2.3 Hz, 1H), 7.55—7.46 (m, 3H), 7.18—7.13 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 170.5, 162.0 (d, *J* = 241 Hz), 155.1 (d, *J* = 12 Hz), 133.4, 131.3, 130.5, 129.1, 127.5, 122.2 (d, *J* = 10 Hz), 113.9 (d, *J* = 25 Hz), 109.4 (d, *J* = 24 Hz); IR (KBr) ν_{max}: 1560, 1455, 1240, 1138, 955, 876, 760, 681 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 229 $[M]^+$, 202, 185, 126, 114, 93, 69.

5-Chloro-2-phenylbenzo[*d*]thiazole (4ma).[38] White solid (30 mg, 62%); mp 135—136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.11—8.02 (m, 3H), 7.79 (d, *J* = 8.5 Hz, 1H), 7.50 (d, *J* = 4.6 Hz, 3H), 7.35 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 169.9, 155.0, 133.3, 133.2, 132.3, 131.3, 129.1, 127.6, 125.6, 123.0, 122.3; IR (KBr) ν_{max}: 2889 IR (KBr) ν_{max}: 1266, 959, 756, 676 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 245 $[M]^+$, 210, 142, 122, 107, 77, 69, 63.

5-Bromo-2-phenylbenzo[*d*]thiazole (4na).[31d] White solid (32 mg, 55%); mp 136—137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.22 (s, 1H), 8.10—8.03 (m, 2H), 7.74 (d, *J* = 8.5 Hz, 1H), 7.55—7.44 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 169.7, 155.3, 133.8, 133.2, 131.3, 129.1, 128.3, 127.6, 126.1, 122.6, 119.9; IR (KBr) ν_{max}: 3072, 1719, 1457, 1255, 961, 880, 747, 690 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 289 $[M]^+$, 210, 188, 146, 108, 77, 69, 63.

4,6-Dimethyl-2-phenylbenzo[*d*]thiazole (4oa).[32a] White solid (37 mg, 78%); mp 85—86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.10 (d, *J* = 6.6 Hz, 2H), 7.55—7.43 (m, 4H), 7.11 (s, 1H), 2.78 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 165.6, 151.6, 135.2, 135.1, 134.1, 132.7, 130.5, 128.9, 128.5, 127.4, 118.7, 21.5, 18.3; IR (KBr) ν_{max}: 3040, 2921, 1666, 1593, 1451, 1320, 12131, 962, 755, 683 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 239 $[M]^+$, 224, 206, 135, 121, 91, 77.

4,6-Dichloro-2-phenylbenzo[*d*]thiazole (4pa).[38] White solid (42 mg, 75%); mp 152—153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.10 (d, *J* = 6.4 Hz, 2H), 7.77 (s, 1H), 7.54—7.46 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 149.9, 137.1, 132.9, 131.6, 130.9, 129.1, 128.5, 127.8, 127.1, 119.8; IR (KBr) ν_{max}: 3076, 1710, 1560, 1446, 1257, 962, 858, 757, 676 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 279 $[M]^+$, 244, 209, 176, 141, 106, 97, 77.

6-Chloro-4-fluoro-2-phenylbenzo[*d*]thiazole (4qa).[38] Yellow solid (30 mg, 57%); mp 156—158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.06 (m, 2H), 7.61 (s, 1H), 7.49 (m, 3H), 7.19 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 168.9, 155.1 (d, *J* = 259 Hz), 141.7 (d, *J* = 13 Hz), 138.2 (d, *J* = 4 Hz), 132.7, 131.5, 131.0 (d, *J* = 9 Hz), 129.0, 127.7, 117.1 (d, *J* = 5 Hz), 113.5 (d, *J* = 21 Hz); IR (KBr) ν_{max}: 3078, 1561, 1437, 1234, 982, 840, 757, 678 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 263 $[M]^+$, 236, 227, 160, 125, 81, 69.

2-Phenylthiazolo[5,4-*c*]pyridine (4ra).[38] White solid (26 mg, 61%); mp 136—137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 9.18 (s, 1H), 8.64 (d, *J* = 5.6 Hz, 1H), 8.19—8.04 (m, 2H), 7.91 (d, *J* = 5.6 Hz, 1H), 7.59—7.43 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 173.3, 158.8, 145.9, 144.1, 132.7, 132.1, 132.0, 129.2, 128.0, 117.3; IR (KBr) ν_{max}: 3031, 1659, 1550, 1462, 1242, 963, 841, 764, 649 cm^{-1}; MS (EI, 70

eV): *m/z* (%) = 212 $[M]^+$, 185, 168, 140, 109, 82, 77.

2-Phenylthiazolo[5,4-*b*]pyridine (4sa). White solid (19 mg, 45%); mp 126—127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.72 (d, *J* = 4.4 Hz, 1H), 8.24 (d, *J* = 8.0 Hz, 1H), 8.21—8.12 (m, 2H), 7.58—7.46 (m, 3H), 7.33—7.26 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 171.2, 164.7, 148.4, 133.0, 131.8, 130.5, 129.0, 128.6, 127.6, 119.8; IR (KBr) ν_{max}: 3051, 1655, 1471, 1379, 1242, 961, 773, 688 cm^{-1}; HRMS-ESI (*m/z*): calcd for $C_{12}H_9N_2S$, $[M+H]^+$: 213.0481, found, 213.0482.

2-(p-Tolyl)benzo[*d*]thiazole (4ab).[38] Yellow solid (40 mg, 88%); mp 85—86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.07 (d, *J* = 8.2 Hz, 1H), 7.99 (d, *J* = 8.1 Hz, 2H), 7.89 (d, *J* = 7.9 Hz, 1H), 7.51—7.45 (m, 1H), 7.37 (dd, *J* = 11.2, 4.0 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 168.2, 154.1, 141.4, 134.9, 130.9, 129.7, 127.5, 126.2, 125.0, 123.0, 121.5, 21.5; IR (KBr) ν_{max}: 3049, 2925, 1473, 1300, 1241, 961, 823, 750 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 225 $[M]^+$, 210, 165, 112, 108, 91, 82, 69.

2-(4-Methoxyphenyl)benzo[*d*]thiazole (4ac).[38] White solid (26 mg, 55%); mp 120—122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.09—8.00 (m, 3H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.49—7.45 (m, 1H), 7.36—7,33 (m, 1H), 6.99 (d, *J* = 8.7 Hz, 2H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 167.8, 161.9, 154.1, 134.8, 129.1, 126.3, 126.2, 124.8, 122.8, 121.5, 114.3, 55.4; IR (KBr) ν_{max}: 3069, 2942, 2835, 1594, 1426, 1248, 1171, 958, 833, 750 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 241 $[M]^+$, 226, 198, 154, 121, 106, 82, 69.

2-(4-Fluorophenyl)benzo[*d*]thiazole (4ad).[29d] Yellow solid (35 mg, 78%); mp 99—100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.13—8.02 (m, 3H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.51—7.48 (m, 1H), 7.40—7.37 (m, 1H), 7.20—7.16 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 166.7, 164.4 (d, *J* = 250 Hz), 154.0, 135.0, 129.9 (d, *J* = 4 Hz), 129.5 (d, *J* = 9 Hz), 126.4, 125.2, 123.2, 121.6, 116.1 (d, *J* = 22 Hz); IR (KBr) ν_{max}: 3062, 2922, 1596, 1479 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 229 $[M]^+$, 202, 185,114, 108, 82, 69, 63.

2-(4-Chlorophenyl)benzo[*d*]thiazole (4ae).[38] White solid (37 mg, 75%); mp 117—118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.07 (d, *J* = 8.2 Hz, 1H), 8.02 (d, *J* = 8.5 Hz, 2H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.54—7.43 (m, 3H), 7.40 (t, *J* = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 166.6, 154.0, 137.0, 135.0, 132.1 129.3, 128.7, 126.5, 125.4, 123.3, 121.6; IR (KBr) ν_{max}: 3058, 1645, 1466, 1286, 1096, 962, 833, 741 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 245 $[M]^+$, 210, 122, 108, 82, 69.

2-(4-Bromophenyl)benzo[*d*]thiazole (4af).[32a] White solid (40 mg, 70%); mp 126—127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.07 (d, *J* = 8.2 Hz, 1H), 7.96 (d, *J* = 8.5 Hz, 2H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 2H), 7.52—7.48 (m, 1H), 7.42—7.38 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 166.7 154.0, 139.0, 135.0, 132.5, 132.2, 128.9, 126.5, 125.4, 123.3, 121.6; IR (KBr) ν_{max}: 1651, 1473, 1251, 960, 832, 744 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 289 $[M]^+$, 210, 183, 145, 108, 105, 82, 69.

2-(4-(Trifluoromethyl)phenyl)benzo[*d*]thiazole (4ag).[30e] White solid (24 mg, 43%); mp 158—159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.20 (d, *J* = 8.0 Hz, 2H), 8.11 (d, *J* = 8.1 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 2H), 7.55—7.51 (m, 1H), 7.45—7.41 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 166.1, 154.0, 136.7, 135.2, 132.5 (q, *J* = 32 Hz), 127.8, 126.7, 126.0 (q, *J* = 4 Hz), 123.8 (q, *J* = 271 Hz), 123.6, 121.7; IR (KBr) ν_{max}: 1649, 1482, 1320, 1115, 963, 839, 750 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 279 $[M]^+$, 260, 240, 210, 140, 108, 82, 69.

4-(Benzo[*d*]thiazol-2-yl)benzonitrile (4ah).[38] White solid (15 mg, 32%); mp 170—171 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.19 (d, *J* = 8.0 Hz, 2H), 8.10 (d, *J* = 8.1 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.55—7.51 (m, 1H), 7.45—7.41 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 165.3, 154.0, 137.4, 135.3, 132.7, 127.9, 126.8, 126.0, 123.8, 121.8, 118.2, 114.1 cm^{-1}; IR (KBr) ν_{max}: 3062, 2225, 1471, 1256, 961, 835, 754; MS (EI, 70 eV): *m/z* (%) = 236 $[M]^+$, 207, 118, 108, 82, 69, 63.

2-(*o*-Tolyl)benzo[*d*]thiazole (4ai).[29f] Yellow solid (20 mg, 45%); mp 37—38 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.12 (d, *J* = 8.2 Hz, 1H), 7.93 (d, *J* = 7.9 Hz, 1H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.56—7.52 (m, 1H), 7.44—7.28 (m, 4H), 2.67 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 168.0, 153.7, 137.2, 135.6, 133.1, 131.5, 130.5, 130.0, 126.1, 126.0, 125.1, 123.3, 121.3, 21.3; IR (KBr) ν_{max}: 3061, 2928, 1851, 1658, 1446, 1297, 1220, 955, 752 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 225 $[M]^+$, 209, 190, 165, 116, 112, 91, 82, 69.

2-(*m*-Tolyl)benzo[*d*]thiazole (4aj).[30e] Yellow solid (23 mg, 50%); mp 68—69 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.12 (d, *J* = 8.2 Hz, 1H), 7.93 (d, *J* = 7.9 Hz, 1H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.56—7.50 (m, 1H), 7.44—7.28 (m, 4H), 2.67 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 168.3, 154.0, 138.8, 135.0, 133.5, 131.8, 128.9, 128.0, 126.3, 125.1, 124.8, 123.1, 121.6, 21.3; IR (KBr) ν_{max}: 3054, 2925, 1684, 1595, 1459, 1304, 1250, 976, 758 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 225 $[M]^+$, 209, 190, 165, 116, 112, 91, 82, 69.

2-(Pyridin-4-yl)benzo[*d*]thiazole (4ak).[29d] White solid (18 mg, 43%); mp 166—167 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.78 (s, 2H), 8.13 (d, *J* = 8.1 Hz, 1H), 7.95 (d, *J* = 5.7 Hz, 3H), 7.57—7.53 (m, 1H), 7.46 (t, *J* = 7.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 165.0, 154.0, 150.6, 140.6, 135.2, 126.8, 126.2, 123.9, 121.8, 121.2; IR (KBr) ν_{max}: 3047, 2925, 1598, 1472, 1414, 1314, 1249, 969, 828, 750 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 212 $[M]^+$, 186, 141, 108, 82, 69.

2-(Thiophen-2-yl)benzo[d]thiazole (4al).[38] White solid (27 mg, 62%); mp 101—103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.04 (d, *J* = 8.2 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 3.5 Hz, 1H), 7.48 (dd, *J* = 14.7, 6.5 Hz, 2H), 7.38—7.34 (m, 1H), 7.14—7.12 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 161.4, 153.6, 137.2, 134.6, 129.3, 128.6, 128.0, 126.4, 125.2, 122.9, 121.4; IR (KBr) ν_{max}: 3073, 2929, 1645, 1429, 1290, 910, 837, 731 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 217 $[M]^+$, 184, 173, 146, 108, 82, 69.

Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.201900340.

Acknowledgement

The authors thank the National Key Research and Development Program of China (No. 2016YFA0602900), the National Natural Science Foundation of China (No. 21420102003), and Guangdong Province Science Foundation (No. 2017B090903003) for financial support.

References

[1] For selected recent examples, see: (a) Zhang, W.; Wang, F.; McCann, S. D.; Wang, D.; Chen, P.; Stahl, S. S.; Liu, G. Enantioselective Cyanation of Benzylic C-H Bonds *via* Copper-Catalyzed Radical Relay. *Science* **2016**, *353*, 1014–1018; (b) Vasilopoulos, A.; Zultanski, S. L.; Stahl, S. S. Feedstocks to Pharmacophores: Cu-Catalyzed Oxidative Arylation of Inexpensive Alkylarenes Enabling Direct Access to Diarylalkanes. *J. Am. Chem. Soc.* **2017**, *139*, 7705–7708; (c) Gini, A.; Brandhofer, T.; Manchenno, O. G. Recent Progress in Mild Csp3-H Bond Dehydrogenative or (Mono-) Oxidative Functionalization. *Org. Biomol. Chem.* **2017**, *15*, 1294–1312; (d) Zhang, H.-J.; Su, F.; Wen, T.-B. Copper-Catalyzed Direct C2-Benzylation of Indoles with Alkylarenes. *J. Org. Chem.* **2015**, *80*, 11322–11329; (e) Paeth, M.; Carson, W.; Luo, J.-G.; Tierney, D.; Cao, Z.; Cheng, M.-J.; Liu, W. Copper-Mediated Trifluoromethylation of Benzylic Csp^3-H Bonds. *Chem. Eur. J.* **2018**, *24*, 11559–11563; (f) Guo, S.; AbuSalim, D. I.; Cook, S. P. Aqueous Benzylic C-H Trifluoromethylation for Late-Stage Functionalization. *J. Am. Chem. Soc.* **2018**, *140*, 12378-12382; (g) Dong, Y.-X.; Li, Y.; Gu, C.-C.; Jiang, S.-S.; Song, R.-J.; Li, J.-H. Copper-Catalyzed Three-Components Intermolecular Alkylesterification of Styrenes with Toluenes and Peroxyeste rs or Acids. *Org. Lett.* **2018**, *20*, 7594–

7597; (h) Soni, V.; Khake, S. M.; Punji, B. Nickel-Catalyzed C(sp^2)-H/C(sp^3)-H Oxidative Coupling of Indoles with Toluene Derivatives. *ACS Catal*. **2017**, *7*, 4202–4208; (i) Ai, F.; Xie, Z.; Jiang, G.; Ji, J.; Le, C. Benzylic C(sp^3)-H Functionalization Reaction of 2-Methylazaarenes in Ionic Liquid Aqueous Solution. *Chin*. *J*. *Org*. *Chem*. **2018**, *38*, 2174–2181; (j) Jiang, X.; Wang, S.; Guo, G.; Lu, B. Recent Development of Metal-Free Direct Asymmetric Functionalization of Benzylic C(sp^3)-H Bond. *Chin*. *J*. *Org*. *Chem*. **2017**, *37*, 841–857; (k) Pei, P.; Zhang, F.; Yi, H.; Lei, A. Visible Light Promoted Benzylic Csp^3-H Bond Activation and Functionalization. *Acta Chim*. *Sinica* **2017**, *75*, 15–21.

[2] For selected recent examples, see: (a) Zhang, X.; Wang, M.; Li, P.; Wang, L. *n*-Bu_4NI/TBHP-catalyzed direct amination of allylic and benzylic C(sp^3)-H with anilines under metal-free conditions. *Chem*. *Commun*. **2014**, *50*, 8006–8009; (b) Pandey, G.; Laha, R. Visible-Light-Catalyzed Direct Benzylic C(sp^3)-H Amination Reaction by Cross-Dehydrogenative Coupling. *Angew*. *Chem*. *Int*. *Ed*. **2015**, *54*, 14875–14879; (c) Song, C.; Dong, X.; Yi, H.; Chiang, C.-W.; Lei, A. DDQ-Catalyzed Direct C(sp^3)-H Amination of Alkylheteroarenes: Synthesis of Biheteroarenes under Aerobic and Metal-Free Conditions. *ACS Catal*. **2018**, *8*, 2195–2199; (d) Brandhofer, T.; Özdemir, A.; Gini, A.; Mancheño, O. G. Double Cu-Catalyzed Direct Csp^3-H Azidation/CuAAC Reaction: A Direct Approach towards Demanding Triazole Conjugates. *Chem*. *Eur*. *J*. **2019**, *25*, 4077–4086; (e) Rabet, P. T. G.; Fumagalli, G.; Boyd, S.; Greaney, M. F. Benzylic C-H Azidation Using the Zhdankin Reagent and a Copper Photoredox Catalyst. *Org*. *Lett*. **2016**, *18*, 1646–1649.

[3] For selected examples, see: (a) Zhang, L.; Yi, H.; Wang, J.; Lei, A. Visible-Light Induced Oxidative Csp^3-H Activation of Methyl Aromatics to Methyl Esters. *Green Chem*. **2016**, *18*, 5122–5126; (b) Li, G.-X.; Morales-Rivera, C. A.; Gao, F.; Wang, Y.; He, G.; Liu, P.; Chen, G. A Unified Photoredox-Catalysis Strategy for C(sp^3)-H Hydroxylation and Amidation Using Hypervalent Iodine. *Chem*. *Sci*. **2017**, *8*, 7180–7185; (c) Choi, D. S.; Ni, Y.; Fernández-Fueyo, E.; Lee, M.; Hollmann, F.; Park, C. B. Photoelectroenzymatic Oxyfunctionalization on Flavin-Hybridized Carbon Nanotube Electrode Platform. *ACS Catal*. **2017**, *7*, 1563–1567; (d) Prier, C. K.; Zhang, R. K.; Buller, A. R.; Brinkmann-Chen, S.; Arnold, F. H. Enantioselective, Intermolecular Benzylic C-H Amination Catalysed by an Engineered Iron-Haem Enzyme. *Nat*. *Chem*. **2017**, *9*, 629–634; (e) Yang, H.; Wang, F.; Jiang, X.; Zhou, Y.; Xu, X.; Tang, P. Silver-Promoted Oxidative Benzylic C-H Trifluoromethoxylation. *Angew*. *Chem*. *Int*. *Ed*. **2018**, *57*, 13266–13270.

[4] For selected examples, see: (a) Huang, X.; Liu, W.; Ren, H.; Neelamegam, R.; Hooker, J. M.; Groves, J. T. Late Stage Benzylic C-H Fluorination with [18F]Fluoride for PET Imaging. *J*. *Am*. *Chem*. *Soc*. **2014**, *136*, 6842–6845; (b) Bloom, S.; McCann, M.; Lectka, T. Photocatalyzed Benzylic Fluorination: Shedding "Light" on the Involvement of Electron Transfer. *Org*. *Lett*. **2014**, *16*, 6338–6341; (c) Nodwell, M. B.; Bagai, A.; Halperin, S. D.; Martin, R. E.; Knust, H.; Britton, R. Direct Photocatalytic Fluorination of Benzylic C-H Bonds with *N*-fluorobenzenesulfonimide. *Chem. Commun*. **2015**, *51*, 11783–11786; (d) West, J. G.; Bedell, T. A.; Sorensen, E. J. The Uranyl Cation as a Visible-Light Photocatalyst for C(sp^3)-H Fluorination. *Angew*. *Chem*. *Int*. *Ed*. **2016**, *55*, 8923–8927; (e) Combe, S. H.; Hosseini, A.; Parra, A.; Schreiner, P. R. Mild Aliphatic and Benzylic Hydrocarbon C-H Bond Chlorination Using Trichloroisocyanuric Acid. *J*. *Org*. *Chem*. **2017**, *82*, 2407–2413.

[5] (a) Larsen, M. A.; Wilson, C. V.; Hartwig, J. F. Iridium-Catalyzed Borylation of Primary Benzylic C-H Bonds without a Directing Group: Scope, Mechanism, and Origins of Selectivity. *J*. *Am*. *Chem*. *Soc*. **2015**, *137*, 8633–8643; (b) Cho, S. H.; Hartwig, J. F. Iridium-Catalyzed Borylation of Secondary Benzylic C-H Bonds Directed by a Hydrosilane. *J*. *Am*. *Chem*. *Soc*. **2013**, *135*, 8157–8160; (c) Cho, S. H.; Hartwig, J. F. Iridium-Catalyzed Diborylation of Benzylic C-H Bonds Directed by a Hydrosilyl Group: Synthesis of 1,1-Benzyldiboronate Esters. *Chem*. *Sci*. **2014**, *5*, 694–698.

[6] Kakiuchi, F.; Tsuchiya, K.; Matsumoto, M.; Mizushima, E.; Chatani, N. $Ru_3(CO)_{12}$-Catalyzed Silylation of Benzylic C-H Bonds in Arylpyridines and Arylpyrazoles with Hydrosilanes via C-H Bond Cleavage. *J*. *Am*. *Chem*. *Soc*. **2004**, *126*, 12792–12793.

[7] Xia, J.-B.; Zhu, C.; Chen, C. Visible Light-Promoted Metal-Free C-H Activation: Diarylketone-Catalyzed Selective Benzylic Mono- and Difluorination. *J*. *Am*. *Chem*. *Soc*. **2013**, *135*, 17494–17500.

[8] Xu, P.; Guo, S.; Wang, L.; Tang, P. Silver-Catalyzed Oxidative Activation of Benzylic C-H Bonds for the Synthesis of Difluoromethylated Arenes. *Angew*. *Chem*. *Int*. *Ed*. **2014**, *53*, 5955–5958.

[9] (a) Hua, A. M.; Bidwell, S. L.; Baker, S. I.; Hratchian, H. P.; Baxter, R. D. Experimental and Theoretical Evidence for Nitrogen–Fluorine Halogen Bonding in Silver-Initiated Radical Fluorinations. *ACS Catal*. **2019**, *9*, 3322–3326; (b) Hua, A. M.; Mai, D. N.; Martinez, R.; Baxter, R. D. Radical C–H Fluorination Using Unprotected Amino Acids as Radical Precursors. *Org*. *Lett*. **2017**, *19*, 2949–2952.

[10] (a) Neil Palmer, W.; Zarate, C.; Chirik, P. J. Benzyltriboronates: Building Blocks for Diastereoselective Carbon-Carbon Bond Formation. *J*. *Am*. *Chem*. *Soc*. **2017**, *139*, 2589–2592; (b) Neil Palmer, W.; Obligacion, J. F.; Pappas, I.; Chirik, P. J. Cobalt-Catalyzed Benzylic Borylation: Enabling Polyborylation and Functionalization of Remote, Unactivated C(sp^3)-H Bonds. *J*. *Am*. *Chem*. *Soc*. **2016**, *138*, 766–769.

[11] Kumar, Y.; Shaw, M.; Thakur, R.; Kumar, A. Copper(II)-Mediated Aerobic Oxidation of Benzylimidates: Synthesis of Primary α-Ketoamides. *J*. *Org*. *Chem*. **2016**, *81*, 6617–6625.

[12] Wang, H.; Wang, Z.; Huang, H.; Tan, J.; Xu, X. KOtBu-Promoted Oxidation of (Hetero)benzylic Csp^3-H to Ketones with Molecular Oxygen. *Org*. *Lett*. **2016**, *18*, 5680–5683.

[13] Lesieur, M.; Genicot, C.; Pasau, P. Development of a Flow Photochemical Aerobic Oxidation of Benzylic C-H Bonds. *Org*. *Lett*. **2018**, *20*, 1987–1990.

[14] Muhldorf, B.; Wolf, R. Photocatalytic benzylic C-H bond oxidation with a flavin scandium complex. *Chem*. *Commun*. **2015**, *51*, 8425–8428.

[15] Hruszkewycz, D. P.; Miles, K. C.; Thiel, O. R.; Stahl, S. S. Co/NHPI-Mediated Aerobic Oxygenation of Benzylic C-H Bonds in Pharmaceutically Relevant Molecules. *Chem*. *Sci*. **2017**, *8*, 1282–1287.

[16] Pipaliya, B. V.; Chakraborti, A. K. Cross-Dehydrogenative Coupling of Heterocyclic Scaffolds with Unfunctionalized Aroyl Surrogates by Palladium(II) Catalyzed C(sp^2)-H Aroylation through Organocatalytic Dioxygen Activation. *J*. *Org*. *Chem*. **2017**, *82*, 3767–3780.

[17] Xie, Y.; Yang, Y.; Huang, L.; Zhang, X.; Zhang, Y. Pd-Catalyzed Arylation/Oxidation of Benzylic C-H Bond. *Org*. *Lett*. **2012**, *14*, 1238–1241.

[18] Guin, S.; Rout, S. K.; Banerjee, A.; Nandi, S.; Patel, B. K. Four Tandem C-H Activations: A Sequential C-C and C-O Bond Making via a Pd-Catalyzed Cross Dehydrogenative Coupling (CDC) Approach. *Org*. *Lett*. **2012**, *14*, 5294–5297.

[19] Zhao, D.; Shen, Q.; Li, J.-X. Potassium Iodide-Catalyzed Three-Component Synthesis of 2-Arylquinazolines via Amination of Benzylic C-H Bonds of Methylarenes. *Adv*. *Synth*. *Catal*. **2015**, *357*, 339–344.

[20] Minami, Y.; Yamada, K.; Hiyama, T. Palladium-Catalyzed Hydrobenzylation of ortho-Tolyl Alkynyl Ethers by Benzylic C-H Activation: Remarkable Alkynoxy-Directing Effect. *Angew*. *Chem*. *Int*. *Ed*. **2013**, *52*, 10611–10615.

[21] Takemoto, S.; Shibata, E.; Nakajima, M.; Yumoto, Y.; Shimamoto, M.; Matsuzaka, H. Ruthenium-Sulfonamide-Catalyzed Direct Dehydrative Condensation of Benzylic C-H Bonds with Aromatic Aldehydes. *J*. *Am*. *Chem*. *Soc*. **2016**, *138*, 14836–14839.

[22] Gao, X.; Zhang, F.; Deng, G.; Yang, L. Brønsted Acid Catalyzed Benzylic C-H Bond Functionalization of Azaarenes: Nucleophilic Addition to Nitroso Compounds. *Org*. *Lett*. **2014**, *16*, 3664–3667.

[23] Mahesh, D.; Satheesh, V.; Kumar, S. V.; Punniyamurthy, T. Copper(II)-Catalyzed Oxidative Coupling of Anilines, Methyl Arenes, and TMSN3 via C(sp^3/sp^2)–H Functionalization and C–N Bond Formation *Org*. *Lett*. **2017**, *19*, 6554–6557.

[24] Yuan, J.; Ma, X.; Yi, H.; Liu, C.; Lei, A. I_2-Catalyzed Oxidative C(sp^3)-H/S-H Coupling: Utilizing Alkanes and Mercaptans as the Nucleophiles. *Chem*. *Commun*. **2014**, *50*, 14386–14389.

[25] (a) Chen, C.; Xu, X.-H.; Yang, B.; Qing, F.-L. Copper-Catalyzed Direct Trifluoromethylthiolation of Benzylic C-H Bonds *via* Nondirected Oxidative C(sp^3)-H Activation. *Org*. *Lett*. **2014**, *16*, 3372–3375; (b) Yang, J.; Hu, J.; Huang, Y.; Xu, X.; Qing, F.-L. Direct Triflylation of Benzylic C-H Bonds with Pyridine as a Directing Group. *Chin*. *J*. *Chem*. **2017**, *35*, 867–870.

[26] Gong, X.; Chen, J.; Lai, L.; Cheng, J.; Sun, J.; Wu, J. Benzylic C(sp^3)-H Bond Sulfonylation of 4-Methylphenols with the Insertion of Sulfur Dioxide under Photocatalysis. *Chem*. *Commun*. **2018**, *54*, 11172–11175.

[27] Yu, H.; Li, Z.; Bolm, C. Nondirected Copper-Catalyzed Sulfoxidations of Benzylic C-H Bonds. *Org*. *Lett*. **2018**, *20*, 2076–2079.

[28] For selected examples, see: (a) Wang, X.; Liu, Q.; Yan, H.; Liu, Z.; Yao, M.; Zhang, Q.; Gong, S.; He, W. Piezochromic Luminescence Behaviors of Two New Benzothiazole-Enamido Boron Difluoride Complexes: Intra- and Inter-molecular Effects Induced by Hydrostatic Compression. *Chem*. *Commun*. **2015**, *51*, 7497–7500; (b) Noel, S.; Cadet, S.; Gras, E.; Hureau, C. The Benzazole Scaffold: a SWAT to Combat Alzheimer's Disease. *Chem*. *Soc*. *Rev*. **2013**, *42*, 7747–7762; (c) Weekes, A. A.; Westwell, A. D. 2-Arylbenzothiazole as a Privileged Scaffold in Drug Discovery. *Curr*. *Med*. *Chem*. **2009**, *16*, 2430–2440.

[29] For selected recent examples, see: (a) Wade, A. R.; Pawar, H. R.; Biware, M. V.; Chikate, R. C. Synergism in semiconducting nanocomposites: visible light photocatalysis towards the formation of C-S and C-N bonds. *Green Chem*. **2015**, *17*, 3879–3888; (b) Sun, Y.; Jiang, H.; Wu, W.; Zeng, W.; Wu, X. Copper-Catalyzed Synthesis of Substituted Benzothiazoles via Condensation of 2-Aminobenzenethiols with Nitriles. *Org*. *Lett*. **2013**, *15*, 1598–1601; (c) Zhu, T.-H.; Wang, S.-Y.; Wang, G.-N.; Ji, S.-J. Cobalt-Catalyzed Oxidative Isocyanide Insertion to Amine-Based Bisnucleophiles: Diverse Synthesis of Substituted 2-Aminobenzimidazoles, 2-Aminobenzothiazoles, and 2-Aminobenzoxazoles. *Chem*. *Eur*. *J*. **2013**, *19*, 5850–5853; (d) Liao, Y.; Qi, H.; Chen, S.; Jiang, P.; Zhou, W.; Deng, G.-J. Efficient 2-Aryl Benzothiazole Formation from Aryl Ketones and 2-Aminobenzenethiols under Metal-Free Conditions. *Org*. *Lett*. **2012**, *14*, 6004–6007; (e) Das, K.; Mondal, A.; Srimani, D. Phosphine Free Mn-Complex Catalyzed Dehydrogenative C-C and C-Heteroatom Bond Formation: A Sustainable Approach to Synthesize Quinoxaline, Pyrazine, Benzothiazole and Quinoline Derivatives. *Chem*. *Commun*. **2018**, *54*, 10582–10585; (f) Natarajan, P.; Muskan, M.; Brar, N. K.; Kaur, J. J. Visible Light Photoredox Catalysis: Conversion of a Mixture of Thiophenols and Nitriles into 2-Substituted Benzothiazoles *via* Consecutive C-S and C-N Bond Formation Reactions. *Org*. *Chem*. *Front*. **2018**, *5*, 1527–1531.

[30] For selected examples, see: (a) Matsushita, K.; Takise, R.; Hisada, T.; Suzuki, S.; Isshiki, R.; Itami, K.; Muto, K.; Yamaguchi, J. Pd-Catalyzed Decarbonylative C-H Coupling of Azoles and Aromatic Esters. *Chem*. *Asian J*. **2018**, *13*, 2393–2396; (b) Ranjit, S.; Liu, X. Direct Arylation of Benzothiazoles and Benzoxazoles with Aryl Boronic Acids. *Chem*. *Eur*. *J*. **2011**, *17*, 1105–1108; (c) Tamba, S.; Okubo, Y.; Tanaka, S.; Monguchi, D.; Mori, A. Palladium-Catalyzed C-H Functionalization of Heteroarenes with Aryl Bromides and Chlorides. *J*. *Org*. *Chem*. **2010**, *75*, 6998–7001; (d) Song, Q.; Feng, Q.; Zhou, M. Copper-Catalyzed Oxidative Decarboxylative Arylation of Benzothiazoles with Phenylacetic Acids and α-Hydroxyphenylacetic Acids with O_2 as the Sole Oxidant. *Org*. *Lett*. **2013**, *15*, 5990–5993; (e) Yang, F.; Koeller, J.; Ackermann, L. hotoinduced Copper-Catalyzed C-H Arylation at Room Temperature. *Angew*. *Chem*. *Int*. *Ed*. **2016**, *55*, 4759–4762.

[31] For selected examples, see: (a) Zhang, G.; Liu, C.; Yi, H.; Meng, Q.; Bian, C.; Chen, H.; Jian, J.-X.; Wu, L.-Z.; Lei, A. External Oxidant-Free Oxidative Cross-Coupling: A Photoredox Cobalt-Catalyzed Aromatic C-H Thiolation for Constructing C-S Bonds. *J*. *Am*. *Chem*. *Soc*. **2015**, *137*, 9273–9280; (b) Wang, H.; Wang, L.; Shang, J.; Li, X.; Wang, H.; Gui, J.; Lei, A. Fe-Catalysed Oxidative C-H Functionalization/C-S Bond Formation. *Chem*. *Commun*. **2012**, *48*, 76–78; (c) Cheng, Y.; Yang, J.; Qu, Y.; Li, P. Aerobic Visible-Light Photoredox Radical C-H Functionalization: Catalytic Synthesis of 2-Substituted Benzothiazoles. *Org*. *Lett*. **2012**, *14*, 98–101; (d) Inamoto, K.; Hasegawa, C.; Kawasaki, J.; Hiroya, K.; Doi, T. Use of Molecular Oxygen as a Reoxidant in the Synthesis of 2-Substituted Benzothiazoles via Palladium-Catalyzed C-H Functionalization/Intramolecular C-S Bond Formation. *Adv*. *Synth*. *Catal*. **2010**, *352*, 2643–2655; (e) Inamoto, K.; Hasegawa, C.; Hiroya, C.; Doi, T. Palladium-Catalyzed Synthesis of 2-Substituted Benzothiazoles *via* a C–H Functionalization/Intramolecular C-S Bond Formation Process. *Org*. *Lett*. **2008**, *10*, 5147–5150; (f) Evindar, G.; Batey, R. A. Parallel Synthesis of a Library of Benzoxazoles and Benzothiazoles Using Ligand-Accelerated Copper-Catalyzed Cyclizations of ortho-Halobenzanilides. *J*. *Org*. *Chem*. **2006**, *71*, 1802–1808; (g) Xu, Z.-M.; Li, H.-X.; Young, D. J.; Zhu, D.-L.; Li, H.-Y.; Lang, J.-P. Exogenous Photosensitizer-, Metal-, and Base-Free Visible-Light-Promoted C-H Thiolation *via* Reverse Hydrogen Atom Transfer. *Org*. *Lett*. **2019**, *21*, 237–241.

[32] (a) Deng, H.; Li, Z.; Ke, F.; Zhou, X. Cu-Catalyzed Three-Component Synthesis of Substituted Benzothiazoles in Water. *Chem*. *Eur*. *J*. **2012**, *18*, 4840–4843; (b) Che, X.; Jiang, J.; Xiao, F.; Huang, H.; Deng, G.-J. Assembly of 2-Arylbenzothiazoles through Three-Component Oxidative Annulation under Transition-Metal-Free Conditions. *Org*. *Lett*. **2017**, *19*, 4576–4579; (c) Nguyen, T. B.; Ermolenko, L.; Retailleau, P.; Al-Mourabit, A. Elemental Sulfur Disproportionation in the Redox Condensation Reaction between *o*-Halonitrobenzenes and Benzylamines. *Angew*. *Chem*. *Int*. *Ed*. **2014**, *53*, 13808–13812; (d) Nguyen, L. A.; Ngo, Q. A.; Retailleau, P.; Nguyen, T. B. Elemental sulfur as a polyvalent reagent in redox condensation with *o*-chloronitrobenzenes and benzaldehydes: three-component access to 2-arylbenzothiazoles. *Green Chem*. **2017**, *19*, 4289–4293; (e) Xing, Q.; Ma, Y.; Xie, H.; Xiao, F.; Zhang, F.; Deng, G.-J. *J*. *Org*. *Chem*. **2019**, *84*, 1238; (f) Zhang, L. F.; Ni, Z. H.; Li, D. Y.; Qin, Z. H.; Wei, X. Y. Convenient synthesis of 2-arylbenzothiazoles and 2-arylnaphthothiazoles. *Chin*. *Chem*. *Lett*. **2012**, *23*, 281–284; (g) Mirller, A.; und Siegjriecl H'ebzr, Y. S. Darstellung von substituierten 2-Aryl(Hetary)-naphtho-[1,2-d] thiazolen. *Z*. *Chem.* **1985**, *25*, 23–24.

[33] Itoh, T.; Mase, T. A Novel Practical Synthesis of Benzothiazoles *via* Pd-Catalyzed Thiol Cross-Coupling. *Org*. *Lett*. **2007**, *9*, 3687–3689.

[34] Ma, D.; Xie, S.; Xue, P.; Zhang, X.; Dong, J.; Jiang, Y. Efficient and Economical Access to Substituted Benzothiazoles: Copper-Catalyzed Coupling of 2-Haloanilides with Metal Sulfides and Subsequent Condensation. *Angew*. *Chem*. *Int*. *Ed*. **2009**, *48*, 4222–4225.

[35] Prasad, D. J. C.; Sekar, G. Cu-Catalyzed in Situ Generation of Thiol Using Xanthate as a Thiol Surrogate for the One-Pot Synthesis of Benzothiazoles and Benzothiophenes. *Org*. *Biomol*. *Chem*. **2013**, *11*, 1659–1665.

[36] Zhang, X.; Zeng, W.; Yang, Y.; Huang, H.; Liang, Y. Copper-Catalyzed Double C-S Bonds Formation *via* Different Paths: Synthesis of Benzothiazoles from *N*−Benzyl-2-iodoaniline and Potassium Sulfide. *Org*. *Lett*. **2014**, *16*, 876–879.

[37] Park, N.; Heo, Y.; Kumar, M. R.; Kim, Y.; Song, K. H.; Lee, S. Synthesis of Benzothiazoles through Copper-Catalyzed One-Pot Three-Component Reactions with Use of Sodium Hydrosulfide as a Sulfur Surrogate. *Eur*. *J*. *Org*. *Chem*. **2012**, *2012*, 1984–1993.

[38] Huang, Y.; Yan, D.; Wang, X.; Zhou, P.; Wu, W.; Jiang, H. Controllable Assembly of the Benzothiazole Framework Using a CC Triple Bond as a One-Carbon Synthon. *Chem*. *Commun*. **2018**, *54*, 1742–1745.

[39] Ma, D.; Pan, J.; Yin, L.; Xu, P.; Gao, Y.; Yin, Y.; Zhao, Y. Copper-Catalyzed Direct Oxidative C–H Functionalization of Unactivated Cycloalkanes into Cycloalkyl Benzo[b]phosphole Oxides *Org*. *Lett*. **2018**, *20*, 3455–3459.

[40] Salman, M.; Zhu, Z.-Q.; Huang, Z.-Z. Dehydrogenative Cross-Coupling Reaction between N-Aryl α-Amino Acid Esters and Phenols or Phenol Derivative for Synthesis of α-Aryl α-Amino Acid Esters. *Org*. *Lett*.

2016, *18*, 1526–1529.

[41] (a) Wang, X.; Qiu, X.; Wei, J.; Liu, J.; Song, S.; Wang, W.; Jiao, N. Cu-Catalyzed Aerobic Oxidative Sulfuration/Annulation Approach to Thiazoles *via* Multiple Csp^3-H Bond Cleavage. *Org*. *Lett*. **2018**, *20*, 2632–2636; (b) Dang, P.; Zheng, Z.; Liang, Y. Copper-Catalyzed $C(sp^3)$-S Bond and $C(sp^2)$-S Bond Cross-Coupling of 2-(2-Iodobenzoyl) Substituted or 2-(2-Iodobenzyl) Substituted 1,2,3,4-Tetrahydroisoquinolines with Potassium Sulfide: Synthesis of Isoquinoline-Fused 1,3-Benzothiazine Scaffolds. *J*. *Org*. *Chem*. **2017**, *82*, 2263–2268.

[42] Yu, W.; Huang, Y.; Li, J.; Tang, X.; Wu, W.; Jiang, H. Copper-Catalyzed Aerobic Oxidative [3+2] Annulation for the Synthesis of 5−Amino/Imino-Substituted 1,2,4-Thiadiazoles through C-N/N-S Bond Formation. *J*. *Org*. *Chem*. **2018**, *83*, 9334–9343.

Manuscript received: August 23, 2019
Manuscript revised: September 11, 2019
Manuscript accepted: September 12, 2019
Accepted manuscript online: September 29, 2019
Version of record online: October 4, 2019

