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N-iodosuccinimide involved One-Pot Metal-free Synthesis of 2-Heteroaromatic Benzothiazole Compounds

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A one-pot protocol for the synthesis of structurally diverse 2-hetarylbenzothiazoles via oxidative condensation of sp^3 C-H bond with benzothiazoles has been described. This process is metal free and operationally simple. A series of 2-hetarylbenzothiazoles were prepared in moderate to good yield under mild conditions.

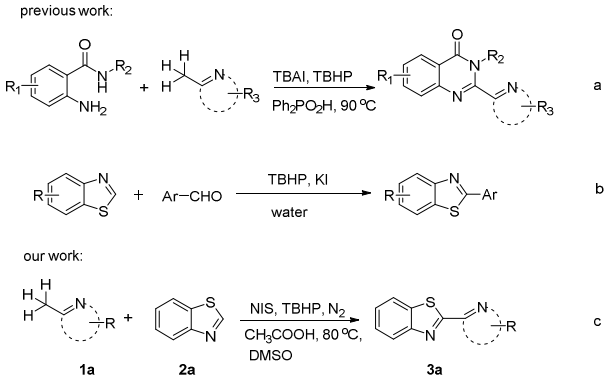
Introduction

2-Substitued benzothiazole derivatives have been reported to present promising activities, such as anti-carcinogenic, antitumor, hydrolyse inhibitors, protease inhibitors[1] and fluorescent dyes.[2]

Traditionally, 2-subsititued benzothiazoles were obtained by condensation of 2-aminothiophenol with aldehydes, carboxylic acids, esters[3] or transition-metal catalysed benzothiazole cross-coupling with aryl halides.[4] 2-Haloanilines as substrate forming 2-substitued benzothiazole was also developed.[5] In 2013, Song et al. reported a Cu-catalyzed oxidative decarboxylative preparation of 2-aryl benzothiazole.[6] Very recently, Wu and co-works described a protocol for the cross-dehydrogenation coupling of quinoline *N*-oxide with benzothiazole affording corresponding 2-subsititued benzothiazole in good yield.[7] However, these transformations suffered from metal contamination, harsh reaction conditions or difficulties in preparation of starting materials. In 2013, Tynebor and co-works reported the synthesis of 2-(1,3-benzothiazol-2-yl)quinolone from aryl tribromomethyl functional group and 2-amino thiophenols.[8] They provided a novel method of synthesis 2-hetarylbenzothiazoles but with a unsatisfied yields. In 2014, we developed a metal-free oxidative amination of sp^3 C-H bond to synthesis 2-hetaryl-quinazolin-4(3*H*)-ones (Scheme 1, a).[9] In 2014, Gao and co-workers developed a KI-catalyzed condensation of arylaldehydes with benzothiazole receiving 2-aryl benzothiazoles (Scheme 1, b).[10] Inspired by these reports, we envision a process for the synthesis of 2-hetarylbenzothiazoles by the oxidative condensation of 2-methylquinoline derivatives with benzothiazoles under mild conditions (Scheme 1, c).

Results and discussion

Scheme 1. Synthesis of 2-hetarylbenzothiazoles



At the outset of our study, we chose 2-methylquinoline (**1a**) and benzothiazole (**2a**) as the model substrates to screen the reaction conditions (Table 1). The reaction was performed at 80 ℃ in DMSO under N_2 atmosphere for 8 hours. Trace amount of target compound was obtained in the absence of iodine source, acid or oxidant (Table 1, entries 1-3). When TBAI, KI were involved in the system, the starting materials afforded trace amounts of the desired product (Table 1, entries 4-5). To our delight, the corresponding product (**3a**) was obtained in a yield of 36% and slightly improved in the presence of NIS (Table 1, entries 6-7). We then investigated several acids. As a result, CH_3COOH proved to be the best acid giving the target molecule in 65% yield (Table 1, entries 8-11). The oxidant was also crucial for this reaction, DPTP and TPBP could promote the transformation with a relatively lower yield (Table 1, entries 12-13). Only trace amounts of desired product was obtained when $K_2S_2O_8$ was used as oxidant (Table 1, entry 14). Finally, if the solvent was changed into toluene, DMF, or PhCl, it caused lower yield of the product (Table 1, entries 15-17).

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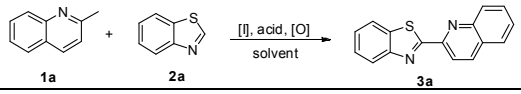
Product 3a could be obtained in 37% yield with longer reaction time (32h) when a catalytic amount of NIS was used (Table 1, entries 18). After completely screened the reaction parameters, the optimized conditions was established as 2-methylquinoline (**1a**) (0.5 mmol), benzothiazole (**2a**) (0.6 mmol), TBHP (2.0 mmol),

Table 1. Optimization of the reaction conditions for the oxidative condensation of 2-methylquinoline (**1a**) with benzothiazole (**2a**)



1a 2a 3a

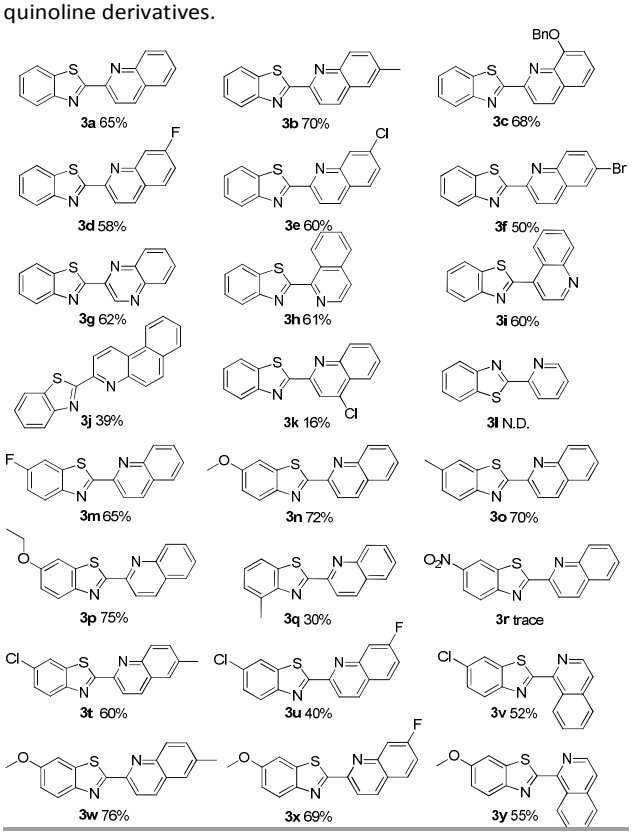
entry	[I]	acid	[O]	solvent	yield, %[b]
1	TBAI	—	TBHP	DMSO	trace
2	—	Ph_2PO_2H	TBHP	DMSO	none
3	TBAI	Ph_2PO_2H	—	DMSO	trace
4	TBAI	Ph_2PO_2H	TBHP	DMSO	trace
5	KI	Ph_2PO_2H	TBHP	DMSO	trace
6	I_2	Ph_2PO_2H	TBHP	DMSO	36
7	NIS	Ph_2PO_2H	TBHP	DMSO	57
8	**NIS**	**CH_3CO_2H**	**TBHP**	**DMSO**	**65**
9	NIS	CF_3CO_2H	TBHP	DMSO	62
10	NIS	$TsOH·H_2O$	TBHP	DMSO	63
11	NIS	PivOH	TBHP	DMSO	60
12	NIS	CH_3CO_2H	DTBP	DMSO	50
13	NIS	CH_3CO_2H	TBPB	DMSO	45
14	NIS	CH_3CO_2H	$K_2S_2O_8$	DMSO	trace
15	NIS	CH_3CO_2H	TBHP	toluene	22
16	NIS	CH_3CO_2H	TBHP	DMF	46
17	TBAI	CH_3CO_2H	TBHP	PhCl	23
18[c]	NIS	CH_3CO_2H	TBHP	DMSO	37

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), acid (0.5 mmol), [I] (0.5 mmol), [O] (2 mmol) and solvent (1.5 mL), 80 °C, under N_2, 8 h. [b]Isolated yield. [c][I] (0.05 mmol), 32 h.

NIS (0.5 mmol) and CH_3COOH (0.5 mmol) at 80 ℃ in DMSO (1.5 mL) under a N_2 atmosphere. The target molecule **3a** was obtained in 65% yield (Table 1, entry 8).

With the optimized reaction conditions in hand, the substrate scope of this method was investigated. Various 2-heteroaromatic benzothiazole Compounds were obtained in fair to good yield (Scheme 2). For the substituted 2-methylquinoline, both electron-donating groups and electron-withdrawing groups could smoothly gave target molecules. Generally, electron-donating groups on the quinoline ring gave higher yields than those with electron-withdrawing groups (Scheme 2, **3a-3f**). When 2-methylquinoxaline, 1-methylisoquinoline, 4-methylquinoline was used as starting material, the corresponding product was also obtained in moderate yields (Scheme 2, **3g-3i**). In addition, quinoline derived from 3-methylbenzo[*f*]quinoline was also compatibly gave the product in 39% yield (Scheme 2, **3j**). However, under the optimized conditions, only 16% yield of **3k** was observed when 4-chloro-2-methylquinoline was employed as reaction substrate. Regretfully, 2-methylpyridine could not convert to the corresponding product (Scheme 2, **3l**). Then, we tried to use 3- and 4-methylpyridine and 3-methylquinoline as substrates, the reactants were recovered and no desired product generated. We also tried to use more convenient and practicable 2-amino thiophenols as substrates oxidative condensation with 4-methylquinoline, 2,6-dimethylquinoline and 1-methylisoquinoline, but the corresponding product was obtained in lower yield 52%, 30% and 45% respectively. Next, various benzothiazoles were coupled with 2-methylquinoline to give the corresponding molecule smoothly. Substrates with an electron-donating substituent afforded higher yield than that with an electron-withdrawing substituent (Scheme 2, **3m-3p**). When substituent placed at the C_4 position, the yield was relatively lower than that at C_6 position (Scheme 2, **3q**). Strong electron-withdrawing substituent such as $–NO_2$ could not give corresponding product (Scheme 2, **3r**), We speculate that Strong electron-withdrawing substituent has significant effect on the oxidative condensation process. 6-Methoxy and 6-chloro benzothiazole were discovered to work efficiently with electron-donating and electron-withdrawing substitued quinolines (Scheme 2, **3t-3y**).

Scheme 2. Oxidative condensation of benothiazoles with quinoline derivatives.



Control experiments were achieved to gain more insight into the reaction mechanism (Scheme 3). Under the optimized reaction conditions, 2-aminobenzenethiol was treated with 2-

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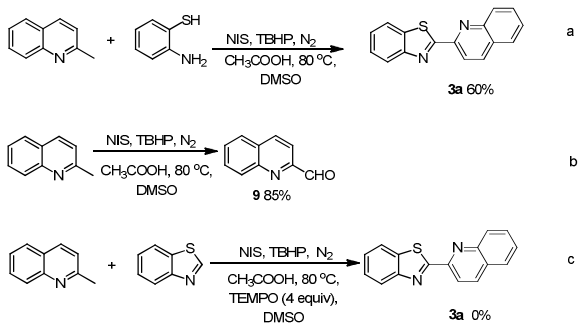
methylquinoline affording **3a** in 60% yield (Scheme 3, a). 2-Methylquinoline could afford quinoline-2-carbaldehyde in 85% yield under the standard conditions (Scheme 3, b). When 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) was added into the reaction system, no desired product was observed. This indicated the reaction might undergo a radical process (Scheme 3, c).



Scheme 3. Control experiments.

Based on the above results and literature reports, we proposed a plausible pathway for the reaction (Scheme 4). In initially, TBHP was decomposed by iodide to obtain tert-butoxyl **A** and tert-butylperoxy radical **B**. 2-Methylquinoline isomerized into **1a'**. methylpyridine and 3-methylquinoline may be difficult to perform the dearomatization process. So, no desired product generated.. Then, addition of a RO radical with **1a'** formed the radical **4**. Radical **4** was further oxidized to give intermediate **5**. After that, intermediate **5** was isomerized and oxidized to form acetal **8.** Hydrolysis of acetal led to the formation of quinoline-2-carbaldehyde **9**. With the assistant of acid, the benzothiazole ring was opened, forming 2-aminothiophenol **2a'**.[6] Finally, oxidative condensation **2a'** with **9** afforded **3a**.

Conclusions

In conclusion, we have developed a method for the synthesis of 2-hetarylbenzothiazoles by the oxidative condensation of 2-methylquinoline derivatives with benzothiazoles involved with NIS-TBHP. This method furnished a one-pot, metal-free and simple strategy for the preparation of 2-hetarylbenzothiazoles.

Acknowledgements

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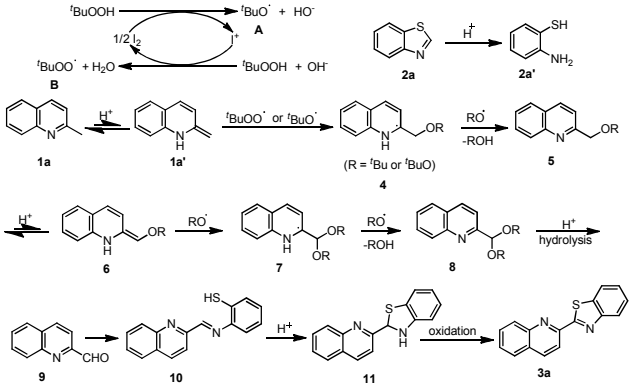
Experimental

Substitued benzothiazoles were obtained according to the literature reports.[11] 6-Ethoxybenzo[d]thiazole and 4-methylbenzo[d]thiazole were also obtained using the same way according to the reference 11. Other reagents and solvents were commercially available and used directly without further purification. All reactions were monitored by TLC. ^{1}H NMR spectra were recorded on a Bruker Avance 400 or 300 spectrometer at 400 or 300 MHz, using $CDCl_3$ as solvent and tetramethylsilane (TMS) as internal standard. ^{13}C NMR spectra were run in the same instrument at 100 or 75 MHz. HRMS spectra were measured on a Q-TOF instrument in positive-ion mode with an ESI ion source.

Scheme 4. Proposed reaction mechanism



Typical Procedure for the Synthesis of 3

A mixture of 2-methylquinoline (**1a**) (0.5 mmol, 0.072 g), benzothiazole (**2a**) (0.6 mmol, 0.081 g), TBHP (2.0 mmol, 0.257 g), NIS (0.5 mmol, 0.112 g) and CH_3COOH (0.5 mmol, 0.003 g) in DMSO (1.5 mL) was stirred at 80 °C under a nitrogen atmosphere until the reaction was completeed (monitored by TLC). The cooled reaction mixture was diluted with brine and saturated $Na_2S_2O_3$ (20 mL) and extracted with ethyl acetate (20 mL×3). The combined organic layers were dried with Na_2SO_4 and evaporated under vacuum to afford the residue. The residue was purified by column chromatography (silica gel) with petroleum ether/ethyl acetate (10: 1) to obtain pure product 3a.

2-(Quinolin-2-yl)benzo[*d*]thiazole 3a[12]. Light yellow solid (65%), M.P.: 178-180 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.51 (d, *J* = 8.4 Hz, 1H), 8.31 (d, *J* = 8.7 Hz, 1H), 8.22 (d, *J* = 8.4 Hz, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 8.00 (d, *J* = 7.8 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.80 (td, *J* = 8.1, 1,2 Hz, 1H), 7.62 (d, *J* = 7.2 Hz, 1H), 7.57-7.50 (m, 1H), 7.47 (td, *J* = 8.4, 1.2 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 169.85, 154.36, 151.31, 147.91, 137.01, 136.50, 130.11, 129.75, 129.00, 127.74, 127.59, 126.28, 125.88, 123.79, 122.03, 118.36; **HRMS** (ESI) calculated for $C_{16}H_{10}N_2S$ $(M+H)^+$ 263.0637; found: 263.0637.

2-(6-Methylquinolin-2-yl)benzo[*d*]thiazole 3b[12]. White solid (70%), M.P.: 184-186 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.44 (d, *J* = 9.0 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 8.13 (d, *J* = 8.1 Hz, 1H), 8.09 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.59-7.56 (m, 2H), 7.53 (td, *J* = 7.2,

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1,2 Hz, 1H) 7.45 (td, *J* = 8.1, 1.2 Hz, 1H), 2.54 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): *δ* 170.03, 154.37, 150.47, 146.49, 137.75, 136.42, 136.25, 132.41, 129.39, 129.05, 126.60, 126.21, 125.74, 123.69, 121.99, 118.35, 21.73; **HRMS** (ESI) calculated for $C_{17}H_{12}N_2S$ $(M+H)^+$ 277.0794; found: 277.0769.

2-(8-(Benzyloxy)quinolin-2-yl)benzo[*d*]thiazole 3c. White solid (61%), M.P.: 236-238 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 8.52 (d, *J* = 8.5 Hz, 1H), 8.27 (d, *J* = 8.6 Hz, 1H), 8.14 (d, *J* = 8.1 Hz, 1H), 8.00 (d, *J* = 7.9 Hz, 1H), 7.69 (d, *J* = 7.4 Hz, 2H), 7.53-7.41 (m, 6H), 7.38 (d, *J* = 7.3 Hz, 1H), 7.19 (dd, *J* = 6.4, 2.5 Hz, 1H); 5.46 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 170.40, 154.79, 154.38, 150.09, 140.50, 137.26, 136.97, 136.62, 130.35, 128.57,, 127.96, 127.78, 127.13, 126.22, 125.79, 123.71, 122.05, 120.29, 118.66, 112.01, 71.46; **HRMS** (ESI) calculated for $C_{23}H_{16}N_2OS$ $(M+H)^+$ 369.1056; found: 369.1057.

2-(7-Fluoroquinolin-2-yl)benzo[*d*]thiazole 3d. White solid (68%), M.P.: 202-204 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): *δ* 8.48 (d, *J* = 8.7 Hz, 1H), 8.30 (d, *J* = 8.4 Hz, 1H), 8.15 (d, *J* = 8.1 Hz, 1H), 8.00 (d, *J* = 7.8 Hz, 1H), 7.88-7.80 (m, 2H), 7.56 (td, *J* = 7.2, 1,2 Hz, 1H), 7.48 (td, *J* = 7.8, 1.2 Hz, 1H), 7.41 (td, *J* = 8.4, 2.4 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): *δ* 169.38, 165.08 (d, *J* = 247.5 Hz), 154.22, 152.16, 148.93 (d, *J* = 12.8 Hz), 136.95, 136.47, 129.79 (d, *J* = 9.8 Hz), 126.38, 126.04, 125.97, 125.96, 123.83, 122.06, 118.26(d, *J* = 25.5 Hz), 117.74 (d, *J* = 2.4 Hz), 113.41 (d, *J* = 21.0 Hz); **HRMS** (ESI) calculated for $C_{16}H_9N_2SF$ $(M+H)^+$ 281.0543; found: 281.0534.

2-(7-Chloroquinolin-2-yl)benzo[*d*]thiazole 3e. White solid (58%), M.P.: 214-216 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): *δ* 8.52 (d, *J* = 8.7 Hz, 1H), 8.30 (d, *J* = 8.7 Hz, 1H), 8.22 (d, *J* = 1.8 Hz, 1H), 8.16 (d, *J* = 8.1 Hz, 1H), 8.01 (d, *J* = 7.5 Hz, 1H), 7.83 (d, *J* = 8.7 Hz, 1H), 7.57-7.51 (m, 2H), 7.49 (td, *J*= 8.1, 1,20 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): *δ* 169.31, 154.25, 152.21, 148.24, 136.88, 136.52, 136.09, 128.91, 128.66, 128.59, 127.31, 126.41, 126.10, 123.87, 122.09, 118.58; **HRMS** (ESI) calculated for $C_{16}H_9N_2SCl$ $(M+H)^+$ 297.0248; found: 297.0229.

2-(6-Bromoquinolin-2-yl)benzo[*d*]thiazole 3f. White solid (60%), M.P.: 240-242 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 8.54 (d, *J* = 8.6 Hz 1H), 8.22 (d, *J* = 8.6 Hz, 1H), 8.16 (d, *J* = 8.1 Hz, 1H), 8.08-8.03 (m, 2H), .8.00 (d, *J* = 7.8 Hz 1H), 7.84 (dd, *J* = 9.0, 2.1 Hz, 1H), 7.56-7.52 (m, 1H), 7.48-7.44 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ*169.27, 154.12, 151.57, 146.45, 136.42, 136.01, 133.67, 131.35, 129.99, 129.83, 126.45, 126.11, 123.83, 122.06, 121.70, 119.33; **HRMS** (ESI) calculated for $C_{16}H_9BrN_2S$ $(M+H)^+$ 340.9743; found: 340.9760.

2-(Quinoxalin-2-yl)benzo[*d*]thiazole 3g[12]. White solid (50%), M.P.: 172-174 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): *δ* 9.88 (s, 1H), 8.22-8.15 (m, 3H), 8.02 (d, *J* = 7.8 Hz, 1H), 7.86-7.80 (m, 2H), 7.59 (td, *J* = 7.5, 1.2 Hz, 1H), 7.51 (td, *J*= 8.1, 1.2 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): *δ* 167.15, 154.41, 146.01, 143..23, 142.95, 141.93, 136.31, 131.04, 130.82, 129.70, 129.50, 126.72, 126.50, 124.23, 122.13; **HRMS** (ESI) calculated for $C_{15}H_9N_3S$ $(M+H)^+$ 264.0589; found: 264.0587.

2-(Isoquinolin-1-yl)benzo[*d*]thiazole 3h[12]. White solid (62%), M.P.: 180-182 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 10.00 (d, *J* = 8.3 Hz, 1H), 8.61 (d, *J* = 5.5 Hz, 1H), 8.20 (d, *J* = 9.3 Hz, 1H), 7.99 (d, *J* = 7.9 Hz, 1H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.79-7.71 (m, 3H), 7.53 (t, *J* = 7.9 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 170.81, 154.84, 149.35, 141.76, 137.28, 136.09, 130.48, 129.01, 127.85, 126.96, 126.07, 125.90, 124.12, 123.01, 121.64; **HRMS** (ESI) calculated for $C_{16}H_{10}N_2S$ $(M+H)^+$ 263.0637; found: 263.0629.

2-(Quinolin-4-yl)benzo[*d*]thiazole 3i[13] white solid (60%), M.P.: 175-177 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): *δ* 9.04-8.99 (m, 2H), 8.24-8.20 (m, 2H), 8.00 (d, *J* = 7.8 Hz, 1H), 7.83-7.76 (m, 2H), 7.71-7.66 (m, 1H), 7.61(t, *J* = 7.5 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 164.75, 154.17, 149.73, 149.17, 138.29, 135.35, 129.97, 129.95, 128.13, 126.71, 126.13, 126.08, 124.97, 124.09, 122.14, 121.59; **HRMS** (ESI) calculated for $C_{16}H_{10}N_2S$ $(M+H)^+$ 263.0637; found: 263.0624.

2-(benzo[f]quinolin-3-yl)benzo[d]thiazole 3j. White solid (39%), M.P.: 232-234 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): *δ* 9.10 (d, *J* = 8.4 Hz, 1H), 8.69-8.62 (m, 2H), 8.16-7.95 (m, 5H), 7.76-7.60 (m, 2H), 7.56 (td, *J* = 7.2, 1.2 Hz, 1H), 7.47-7.42 (m, 1H);**^{13}C NMR** (75 MHz, $CDCl_3$): *δ* 169.75, 154.45, 150.76, 148.03, 136.48, 132.12, 131,66, 131.57, 129.47, 128.83, 128.09, 127.83, 127.38, 126.54, 126.28, 125.77, 123.71, 123.04, 122.03, 118.46; **HRMS** (ESI) calculated for $C_{20}H_{12}N_2S$ $(M+H)^+$ 313.0794; found: 313.0792.

2-(4-Chloroquinolin-2-yl)benzo[*d*]thiazole 3K. White solid (16%), M.P.: 190-192 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): *δ* 8.60 (s, 1H), 8.27 (dd, *J* = 8.4, 0.6 Hz, 1H), 8.22 (d, *J* = 8.2 Hz, 1H), 8.15-8.12 (m, 1H), 7.99 (dd, *J* = 7.5, 0.3 Hz, 1H), 7.84-7.78 (m, 1H), 7.71-7.65 (m, 1H), 7.56 (td, *J* = 7.2, 1.2 Hz, 1H), 7.48 (td, *J* = 7.2, 1.2 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): *δ* 167.48, 153.12, 150.12, 147.56, 142.55, 135.48, 129.91, 129.04, 127.47, 125.99, 125.43, 125.11, 123.24, 122.87, 121.02, 117.46; **HRMS** (ESI) calculated for $C_{16}H_9ClN_2S$ $(M+H)^+$ 297.0248; found: 297.0241.

6-Fluoro-2-(quinolin-2-yl)benzo[*d*]thiazole 3m. Yellow solid (65%), M.P.: 207-209 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): *δ* 8.49 (d, *J* = 8.4 Hz, 1H), 8.33 (d, *J*= 8.7 Hz, 1H), 8.24 (d, *J* = 8.4Hz, 1H), 8.11-8.06 (m, 1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.81-7.76 (m, 1H), 7.68-7.59 (m, 2H), 7.30-7.23 (m,1H); **^{13}C NMR** (75 MHz, $CDCl_3$): *δ* 162.69 (d, *J* = 245.3 Hz); 150.94, 147.79, 137.76 (d, *J* = 11.3 Hz), 137.17, 130.23, 129.63, 128.99, 127.73, 127.70, 124.86 (d, *J* = 9.0 Hz), 118.21, 115.25 (d, *J* = 24.8 Hz), 108.30 (d, *J* = 26.3 Hz); **HRMS** (ESI) calculated for $C_{16}H_9FN_2S$ $(M+H)^+$ 281.0543; found: 281.0563.

6-Methoxy-2-(quinolin-2-yl)benzo[*d*]thiazole 3n[14]. Yellow solid (72%), M.P.: 178-180 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): *δ* 8.46 (d, *J* = 8.7 Hz, 1H), 8.28 (d, *J*= 8.7 Hz, 1H), 8.20 (d, *J*= 8.4 Hz 1H), 8.02 (d, *J* = 9.0 Hz, 1H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.78-7.72 (m, 1H), 7.60-7.54 (m, 1H), 7.43 (d, *J* = 2.7 Hz, 1H), 7.14 (dd, *J* = 9.0, 2.7 Hz, 1H), 3.92 (S, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): *δ* 167.28, 158.41, 151.50, 148.98, 147.93, 138.07, 136.88, 130.02, 129.63, 128.81, 127.71, 127.35, 124.36, 118.18, 116.02, 104.17, 55.81; **HRMS** (ESI) calculated for $C_{17}H_{12}N_2OS$ $(M+H)^+$ 293.0743; found: 293.0763.

6-Methyl-2-(quinolin-2-yl)benzo[*d*]thiazole 3o[15]. Yellow solid (70%), M.P.: 210-212 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): *δ* 8.53 (d, *J* = 8.7 Hz, 1H), 8.32 (d, *J* = 8.4 Hz, 1H), 8.23 (d, *J* = 8.4 Hz 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.78-7.75 (m, 2H), 7.62 (t, *J* = 7.5Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 2.53 (S, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): *δ* 168.77, 152.53, 151.51, 147.94, 136.90, 136.71, 136.17, 130.03, 129.72, 128.93, 127.95, 127.70, 127.44, 123.28, 121.72, 118.34, 21.61; **HRMS** (ESI) calculated for $C_{17}H_{12}N_2S$ $(M+H)^+$ 277.0794; found: 277.0798.

6-Ethoxy-2-(quinolin-2-yl)benzo[*d*]thiazole 3p[14]. Yellow solid (75%), M.P.: 200-202 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 8.44 (d, *J* = 8.4 Hz, 1H), 8.27 (d, *J* = 8.8 Hz, 1H), 8.19 (d, *J* = 8.8 Hz 1H), 8.00 (d, *J* = 9.2 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.76-7.72 (m, 1H), 7.58-7.56 (m, 1H), 7.39 (d, *J* = 2.4 Hz, 1H), 7.11 (dd, *J* = 8.8, 2.4 Hz 1H), 4.15 (q, *J* = 6.8 Hz 2H), 1.48 (t, *J* = 6.8 Hz 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 167.09,

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157.79, 151.46, 148.80, 147.87, 138.04, 136.95, 130.07, 129.60, 128.81, 127.73, 127.38, 124.33, 118.22, 116.45, 104.82, 64.12, 14.85; **HRMS** (ESI) calculated for $C_{18}H_{14}N_2OS$ $(M+H)^+$ 307.09; found: 307.3960.

4-Methyl-2-(quinolin-2-yl)benzo[*d*]thiazole 3q. white solid (30%), M.P.: 172-174 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.57 (d, *J* = 8.8 Hz, 1H), 8.30 (d, *J* = 8.4 Hz, 1H), 8.21 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.82 (dd, *J* = 7.2, 2.0 Hz, 1H), 7.78-7.74 (m, 1H), 7.61-7.57 (m, 1H), 7.35-7.32 (m, 2H), 2.85 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 168.32, 153.83, 151.70, 147.94, 136.85, 136.46, 133.92, 130.02, 129.74, 128.97, 127.74, 127.44, 126.69, 125.81, 119.40, 118.53, 18.28; **HRMS** (ESI) calculated for $C_{17}H_{12}N_2S$ $(M+H)^+$ 277.0794; found: 277.0796.

6-Chloro-2-(6-methylquinolin-2-yl)benzo[*d*]thiazole 3t. yellow solid (60%), M.P.: 212-214 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.43 (d, *J* = 8.7 Hz, 1H), 8.22 (d, *J* = 8.7 Hz, 1H), 8.12 (d, *J* = 8.1 Hz 1H), 8.04 (d, *J* = 8.7 Hz, 1H), 7.95 (d, *J* = 1.8 Hz, 1H), 7.63-7.60 (m, 2H), 7.49 (dd, *J* = 8.7, 1.8 Hz, 1H), 2.57 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 170.33, 152.85, 149.96, 146.29, 138.11, 137.67, 136.56, 132.69, 131.86, 129.24, 129.14, 127.13, 126.64, 124.43, 121.62, 118.32, 21.77; **HRMS** (ESI) calculated for $C_{17}H_{11}ClN_2S$ $(M+H)^+$ 311.0404; found: 311.0410.

6-Chloro-2-(7-fluoroquinolin-2-yl)benzo[*d*]thiazole 3u. white solid (40%), M.P.: 224-226 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.44 (d, *J* = 8.4 Hz, 1H), 8.32 (d, *J* = 8.8 Hz, 1H), 8.05 (d, *J* = 8.8 Hz 1H), 7.97 (d, *J* = 2.0 Hz, 1H), 7.89-7.81 (m, 2H), 7.50 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.41 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 169.99, 169.57, 164.75 (d, *J* = 259.0 Hz), 152.92, 151.91, 148.97 (d, *J* = 13.0 Hz), 137.78, 137.01, 132.11, 129.80 (d, *J* = 10.0 Hz), 127.22, 126.05, 124.62, 121.66, 118.39 (d, *J* = 26.0 Hz), 117.62, 113.41 (d, *J* = 21.0 Hz); **HRMS** (ESI) calculated for $C_{16}H_8ClFN_2S$ $(M+H)^+$ 315.0154; found: 315.0173.

6-Chloro-2-(isoquinolin-1-yl)benzo[*d*]thiazole 3v yellow solid (52%), M.P.: 184-186 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): δ 9.35 (m, 1H), 8.66 (d, *J* = 5.4 Hz, 1H), 8.13 (d, *J* = 8.7 Hz 1H),7.99 (d, *J* = 1.8 Hz, 1H), 7.95-7.92 (m, 1H), 7.85-7.78 (m, 3H), 7.52 (dd, *J* = 8.7, 1.8 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 171.39, 153.36, 148.87, 141.73, 137.32, 132.03, 130.62, 129.15, 127.65, 127.04, 126.92, 126.01, 124.85, 123.28, 121.26; **HRMS** (ESI) calculated for $C_{17}H_9ClN_2S$ $(M+H)^+$ 297.0248; found: 297.0230.

6-Methoxy-2-(6-methylquinolin-2-yl)benzo[*d*]thiazole 3w. yellow solid (76%), M.P.: 188-200 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.45 (d, *J* = 8.4 Hz, 1H), 8.22 (d, *J* = 8.7 Hz, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 9.0 Hz, 1H), 7.62-7.59 (m, 2H), 7.43 (d, *J* = 2.4 Hz, 1H), 7.15 (dd, *J* = 9.0, 2.4 Hz, 1H), 3.92 (s, 3H), 2.57 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 167.01, 158.45, 150.34, 148.68, 146.15, 137.98, 137.76, 136.56, 132.59, 129.06 128.91, 126.65, 124.27, 118.36, 116.15, 104.16, 55.85, 21.74; **HRMS** (ESI) calculated for $C_{18}H_{14}N_2OS$ $(M+H)^+$ 307.09; found: 307.0927.

2-(7-Fluoroquinolin-2-yl)-6-methoxybenzo[*d*]thiazole 3x. yellow solid (69%), M.P.: 201-221 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.46 (d, *J* = 8.4 Hz, 1H), 8.29 (d, *J* = 8.4 Hz, 1H), 8.04 (d, *J* = 9.0 Hz, 1H), 7.88-7.81 (m, 2H), 7.43-7.40 (m, 1H), 7.38 (dd, *J* = 8.7, 2.7 Hz, 1H), 7.16 (dd, J =9.0, 2.4 Hz, 1H), 3.93 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 166.77, 165.11 (d, *J* = 249.2 Hz), 158.58, 152.34, 148.96 (d, *J* = 10.6 Hz), 138.11, 136.85, 129.76 (d, *J* = 9.9 Hz), 125.80, 124.43, 118.02 (d, *J* = 25.4 Hz), 117.62, 117.59, 116.24, 113.33 (d, *J* = 20.6 Hz), 104.14, 55.85; **HRMS** (ESI) calculated for $C_{17}H_{11}FN_2OS$ $(M+H)^+$ 311.0649; found: 311.0669.

2-(Isoquinolin-1-yl)-6-methoxybenzo[*d*]thiazole 3y. yellow solid (55%), M.P.: 200-202 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): δ 9.97-9.94 (m,1H), 8.65 (d, *J* = 5.4 Hz, 1H), 8.11 (d, *J* = 9.0 Hz, 1H), 7.93-7.89 (m, 1H), 7.84-7.78 (m, 3H), 7.45 (d, *J* = 2.4 Hz, 1H), 7.17 (dd, *J* = 9.0, 2.4 Hz, 1H), 3.94 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 158.55, 149.33, 141.33, 137.72, 137.39, 130.69, 129.03, 128.04, 126.97, 125.94, 124.77, 122.72, 116.01, 103.73, 55.83; **HRMS** (ESI) calculated for $C_{17}H_{12}N_2OS$ $(M+H)^+$ 293.0743; found: 293.0726.

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