Synthesis X.-Y. Liu et al. Paper

Insertion Reaction of 2-Halo-*N*-allylanilines with K_2S Involving Trisulfur Radical Anion: Synthesis of Benzothiazole Derivatives under Transition-Metal-Free Conditions

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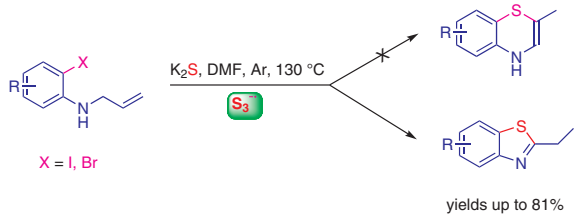

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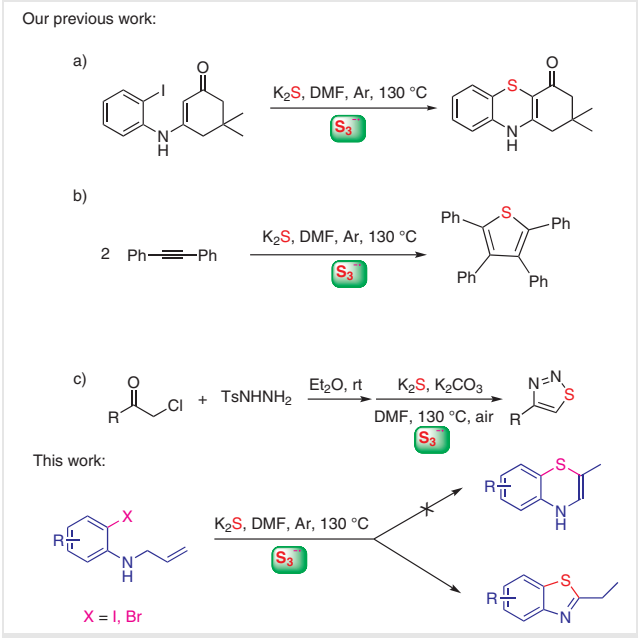
Abstract A synthesis of benzothiazole derivatives through the reaction of 2-halo-*N*-allylanilines with K_2S in DMF is developed. The trisulfur radical anion $S_3^{\cdot-}$, which is generated in situ from K_2S in DMF, initiates the reaction without transition-metal catalysis or other additives. In addition, two C–S bonds are formed and heteroaromatization of benzothiazole is triggered by radical cyclization and H-shift.

Keywords transition metal-free, trisulfur radical anion, benzothiazole derivatives, radicals, cyclization

Benzothiazole is a very important skeleton of organic compounds and it exists in many natural products.[1] The versatile biological activities of benzothiazole compounds lead to their use as medical and biological molecules,[2] and the importance of benzothiazoles has prompted organic chemists to focus on their synthesis. Benzothiazoles are generally obtained by using 2-halobenzothiazole[3] and benzo[*d*]thiazol-2-amine.[4] They can also be synthesized by using aminothiophenol and DMF,[5] CO_2,[6] or CO.[7] Although these methods afford various benzothiazoles, they require unfriendly reaction conditions, such as precious metal catalysts, complex reaction conditions and multiple steps. These drawbacks limit the application of these methods in practice. It is thus desirable to find an environmentally friendly method for the synthesis of benzothiazoles and their derivatives.

$S_3^{\cdot-}$ has attracted significant attention for the synthesis of sulfur-containing compounds in recent years.[8] $S_3^{\cdot-}$ is easily generated in situ from K_2S or S_8 and initiates reactions without transition-metal catalysts. Our groups have developed serial reactions for the construction of different sulfur-containing compounds such as benzothiazine (Scheme 1a),[9] substituted thiophenes (Scheme 1b),[10] as well as 1,2,3-thiadiazole and isothiazole (Scheme 1c).[11]

As part of our continuing interests in C–S bond-formation reactions involving $S_3^{\cdot-}$, we considered whether the reaction of 2-halo-*N*-allylanilines with K_2S in DMF could be

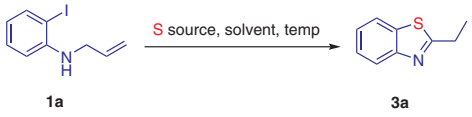


Scheme 1 A proposed route to access unsymmetrical thiosulfonates through insertion of sulfur dioxide

used to construct 4*H*-benzo[*b*][1,4]thiazine derivatives. To our surprise, unexpected benzothiazole derivatives were observed instead of 4*H*-benzo[*b*][1,4]thiazine derivatives. Herein, we offer a new solution for the construction of benzothiazole derivatives via an in situ generated $S_3^{\cdot-}$ initiated reaction of 2-halo-*N*-allylanilines with K_2S in DMF without transition-metal catalyst or other additives.

The study is initiated by the reaction of **1a** (0.5 mmol) with K_2S (2.2 equiv) in DMA (2 mL) at 130 °C under Ar atmosphere. To our surprise, 2-ethylbenzo[*d*]thiazole (**3a**) instead of 2-methyl-4*H*-benzo[*b*][1,4]thiazine was observed in 24% yield (Table 1, entry 1). To optimize the reaction conditions, we screened the reaction of **1a** with K_2S in different solvents such as DMF, DMSO, DCE, CH_3CN, and 1,4-dioxane (entries 2–6). DMF gave the best result and **3a** was obtained in 53% yield. The reaction of **1a** with K_2S did not afford **3a** in DCE, CH_3CN, or 1,4-dioxane. Next, we tried to apply other sulfur sources to replace K_2S (entries 7 and 8); however, it was found that the reaction of **1a** with S_8, $Na_2S_2O_3$ or Cu_2S all failed to give **3a** (entries 7, 8, and 16). When $Na_2S{\cdot}9H_2O$ and $(NH_4)_2S$ instead of K_2S were applied to the reaction, **3a** was observed in lower yields (entries 14 and 15). It should be noted that either increasing or decreasing the amount of K_2S resulted in lower yields of **3a** (entries 9 and 10). When the reaction was carried out under the air atmosphere, no desired product **3a** was observed (entry 11). We also investigated the effect of temperature (entries 12 and 13) but no better results were observed.

Table 1 Optimization of the Reaction Conditions[a]

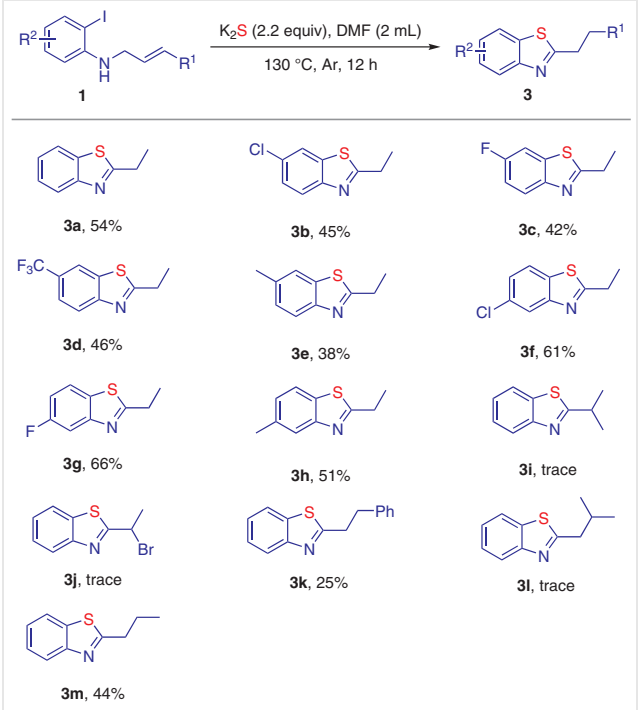


1a **3a**

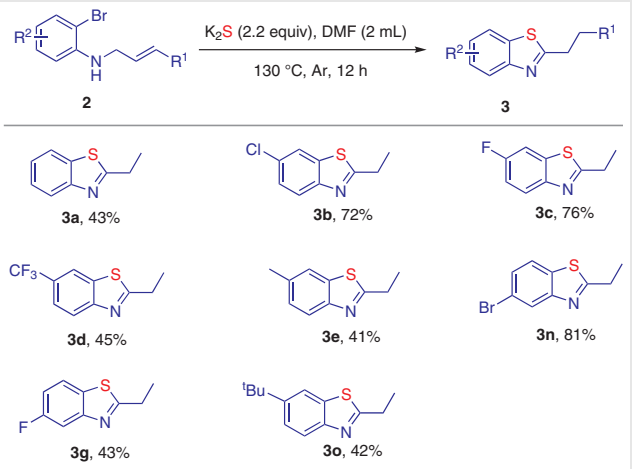
Entry	Solvent (2 mL)	S source (equiv)	Temp (°C)	Yield (%)[b]
1	DMA	K_2S (2.2)	130	24
2	DMF	K_2S (2.2)	130	53
3	DMSO	K_2S (2.2)	130	11
4	DCE	K_2S (2.2)	130	NR
5	MeCN	K_2S (2.2)	130	NR
6	1,4-dioxane	K_2S (2.2)	130	NR
7	DMF	S_8 (2.2)	130	NR
8	DMF	$Na_2S_2O_3$ (1.1)	130	NR
9	DMF	K_2S (2.5)	130	41
10	DMF	K_2S (1.5)	130	trace
11[c]	DMF	K_2S (2.2)	130	NR
12	DMF	K_2S (2.2)	80	NR
13	DMF	K_2S (2.2)	100	trace
14	DMF	$Na_2S{\cdot}9H_2O$	130	32
15	DMF	$(NH_4)_2S$	130	<10
16	DMF	Cu_2S	130	NR

[a] Reaction conditions: **1a** (0.5 mmol), solvent (2 mL), 130 °C, 12 h, under Ar atmosphere.
[b] Isolated yield.
[c] Air atmosphere.

With the optimized conditions in hand, we explored the versatility of the reaction; the results are summarized in Scheme 2. The reaction of *N*-allyl-4-chloro-2-iodoaniline (**1b**) and *N*-allyl-4-fluoro-2-iodoaniline (**1c**) with K_2S worked well to afford **3b** and **3c** in 45% and 42% yield, respectively. Similarly, when *N*-allyl-2-iodo-4-(trifluoromethyl)aniline (**1d**) and *N*-allyl-2-iodo-4-methylaniline (**1e**) were subjected to the reaction under identical conditions, **3d** and **3e** was also observed in 46% and 38% yield, respectively. These results indicate that electronic effects at the 4-position of the aromatic ring has little impact on the reaction. It should be noted that the reaction of *N*-allyl-5-chloro-2-iodoaniline (**1f**) and *N*-allyl-5-fluoro-2-iodoaniline (**1g**) with K_2S also proceeded smoothly to give **3f** and **3g** in 61% and 66% yields, respectively. The reaction of *N*-allyl-2-iodo-5-methylaniline (**1h**) with K_2S led to **3h** in 51% yield. Unfortunately, the reactions of 2-iodo-*N*-(2-methylallyl)aniline (**1i**), *N*-(2-bromoallyl)-2-iodoaniline (**1j**), or 2-iodo-*N*-(3-methylbut-2-en-1-yl)aniline (**1l**) with K_2S failed to furnish the desired products. To our delight, *N*-cinnamyl-



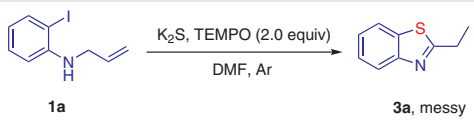
Scheme 2 Substrate scope of 2-iodo-*N*-allylanilines. *Reagents and conditions*: **1** (0.5 mmol), solvent (2 mL), 130 °C, 12 h, under Ar atmosphere. Isolated yields are given.



Scheme 3 Substrate scope of 2-bromo-*N*-allylanilines. *Reagents and conditions*: **1** (0.5 mmol), solvent (2 mL), 130 °C, 12 h, under Ar atmosphere. Isolated yields are given.

2-iodoaniline (**1k**) and (*E*)-*N*-(but-2-en-1-yl)-2-iodoaniline (**1m**) also reacted with K_2S to give **3k** and **3m** in 25% and 44% yield, respectively.

We then investigated the scope of the reaction with respect to 2-bromo-*N*-allylanilines under identical reaction conditions (Scheme 3). It should be noted that the reaction of 2-bromo-*N*-allylanilines **2** with K_2S could also afford benzothiazoles but exhibited different reactivities. The

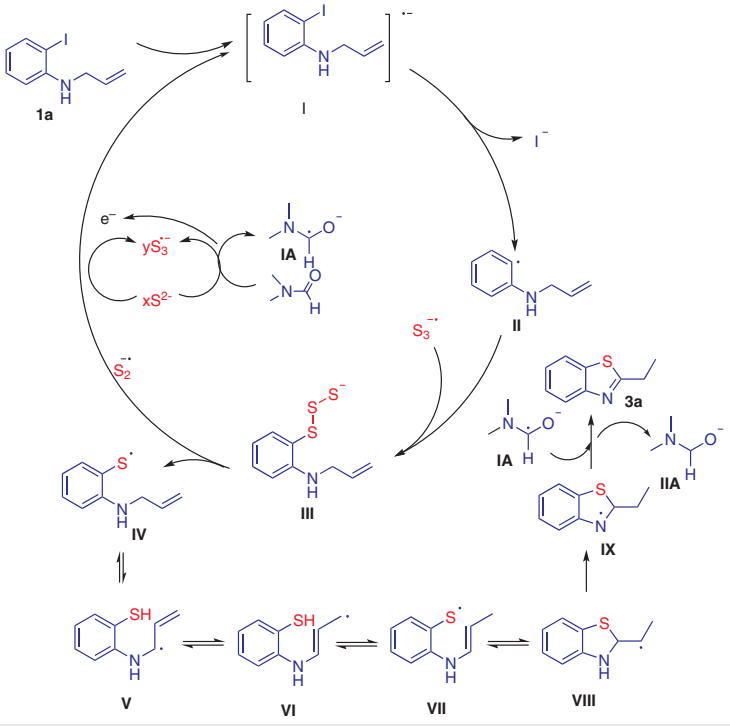


Scheme 4 Control experiment

yield of **3b** could be increased from 45% to 72% yield when *N*-allyl-2-bromo-4-chloroaniline (**2b**) instead of **1b** was applied to the reaction with K_2S. The reaction of *N*-allyl-2-bromo-4-fluoroaniline **2c** with K_2S gave **3c** in 76% yield. It is worth noting that the reaction conditions were also efficient with *N*-allyl-2,5-dibromoaniline **2n**, which chemoselectively afforded **3n** in 81% yield. After that, we also tried the corresponding chlorinated compounds. Although the corresponding products could be obtained, the reaction system was rather messy.

To further understand the reaction mechanism, we tried the reaction of **1a** with K_2S in the presence of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) (Scheme 4). It was found that the reaction was complex and no desired product **3a** was observed. Although it is difficult to confirm whether formation of $S_3^{\cdot-}$ occurred in the TEMPO inhibition experiment, this result indicated that the in situ generated $S_3^{\cdot-}$ from K_2S may be involved and may trigger the reaction.

Based on the above experimental results, and in conjunction with relevant literature,[9] we have proposed a possible reaction mechanism in Scheme 5. First, $S_3^{\cdot-}$ is generat-



Scheme 5 Plausible mechanism

ed in situ by the mixture of K_2S in DMF with release of electrons. The electron reacts with **1a** to give the radical anion intermediate **I**, which releases iodine ion to afford radical **II**. The coupling of radical **II** with $S_3^{\cdot-}$ furnishes **III**, the homolysis of which gives radical **IV** and $S_2^{\cdot-}$. The latter reacts with K_2S to regenerate $S_3^{\cdot-}$. Following a subsequent 1,5-H shift, 1,3-H shift and 1,7-H shift, radical **IV** converts into radical **VII**. The intramolecular cyclization of **VII** leads to radical **VIII**. After 1,3-H shift and heteroaromatization, **3a** is formed.

In summary, a new protocol for the synthesis of benzothiazole derivatives via an in situ generated $S_3^{\cdot-}$ initiated reaction of 2-halo-*N*-allylanilines with K_2S in DMF has been developed that proceeds under simple reaction conditions without transition-metal catalyst or other additives. It is interesting that two C–S bonds are formed and heteroaromatization of benzothiazole is triggered by radical cyclization and H-shift. This study also extends the scope of applications of $S_3^{\cdot-}$ in organic synthesis.

Unless otherwise noted, all commercially available compounds were used as provided without further purification. All the solvents for routine isolation of products and chromatography were reagent grade. Analytical thin-layer chromatography (TLC) was performed on silica gel, with detection by irradiation with UV light. For column chromatography, 300–400 mesh silica gel was used. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker 400 MHz and Bruker 300 MHz spectrometers in $CDCl_3$. Chemical shifts (δ) are reported referenced to an internal tetramethylsilane standard or to the $CDCl_3$ residual peak (δ = 7.26 ppm) for ^{1}H NMR spectra. Chemical shifts of ^{13}C NMR signals are reported relative to $CDCl_3$ (δ = 77.16 ppm). Data are reported as chemical shift (δ in ppm), multiplicity [indicated as s (singlet), bs (broad singlet), d (doublet), t (triplet), m (multiplet)], coupling constant (*J* in Hz). Melting points were measured with an Electrothermal digital melting point apparatus and are uncorrected. IR spectra were recorded with a Bruker Vertex 70 spectrophotometer and are reported in terms of frequency of absorption (cm^{-1}). HRMS spectra were obtained with a GCT Premier TOF-MS with CI source or with a Bruker microTOF-Q III instrument with ESI source.

Synthesis of 1 and 2 (1a, 2a, 2e,[12a] 1b, 1d, 1e,[12b] 1c,[12c] 1i,[12d] 1k,[12e] 1l,[12f] 1m,[12g] 2d,[12h] 2f[12i]); Typical Procedure for 1a

To a solution of 2-iodoaniline (2.4 mmol) and potassium carbonate (4.0 mmol) in DMF (3 mL) was slowly added allyl bromide (2.0 mmol). The mixture was stirred at r.t. for 16 h, then the reaction was quenched with H_2O (15 mL) and the mixture was extracted with EtOAc (3 × 15 mL). The combined organic layer was dried ($MgSO_4$), filtered and evaporated, followed by a silica gel column chromatography (PE) to afford *N*-allyl-2-iodoaniline.

N-Allyl-2-bromo-4-chloroaniline (2b)

Yield: 447 mg (76%); Colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.47–7.40 (m, 1 H), 7.18–7.09 (m, 1 H), 6.59–6.50 (m, 1 H), 6.01–5.85 (m, 1 H), 5.34–5.17 (m, 2 H), 4.47 (s, 1 H), 3.81 (d, *J* = 5.1 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.6, 134.3, 131.8, 128.4, 121.6, 116.8, 112.1, 109.6, 46.4.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C_9H_9BrClN: 245.9680; found: 245.9685.

N-Allyl-2-bromo-4-fluoroaniline (2c)

Yield: 448 mg (82%); Colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25–7.18 (m, 1 H), 6.99–6.89 (m, 1 H), 6.59–6.52 (m, 1 H), 5.96 (m, *J* = 17.2, 10.3, 5.2 Hz, 1 H), 5.34–5.20 (m, 2 H), 4.31 (s, 1 H), 3.80 (m, *J* = 5.3, 1.7 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.6 (d, *J* = 237.0 Hz), 141.6 (d, *J* = 2.3 Hz), 134.7, 119.4 (d, *J* = 24.7 Hz), 116.6, 115.0 (d, *J* = 21.7 Hz), 111.6 (d, *J* = 7.5 Hz), 108.9 (d, *J* = 9.7 Hz), 46.7.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –117.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C_9H_9BrFN: 229.9975; found: 229.9981.

N-Allyl-2-bromo-5-fluoroaniline (2g)

Yield: 400 mg (73%); Colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.30 (m, 1 H), 6.39–6.28 (m, 2 H), 5.94 (m, *J* = 17.2, 10.3, 5.1 Hz, 1 H), 5.35–5.20 (m, 2 H), 4.59 (s, 1 H), 3.81 (m, *J* = 7.1, 3.4, 2.5 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.4 (d, *J* = 242.2 Hz), 146.1 (d, *J* = 11.3 Hz), 134.1, 132.9 (d, *J* = 9.7 Hz), 116.8, 104.4 (d, *J* = 22.5 Hz), 103.7 (d, *J* = 2.2 Hz), 99.1 (d, *J* = 27.7 Hz), 46.2.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –116.4.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C_9H_9BrFN: 229.9975; found: 229.9981.

N-Allyl-2-bromo-4-(*tert*-butyl)aniline (2o)

Yield: 557 mg (87%); Colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.56 (d, *J* = 2.3 Hz, 1 H), 7.30–7.26 (m, 1 H), 6.70–6.66 (m, 1 H), 6.04 (m, *J* = 17.2, 10.3, 5.2 Hz, 1 H), 5.42–5.26 (m, 2 H), 4.44 (s, 1 H), 3.89 (m, *J* = 5.3, 1.7 Hz, 2 H), 1.37 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.5, 141.1, 135.1, 129.4, 125.3, 116.3, 111.4, 109.8, 46.5, 33.9, 31.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{18}BrN$: 268.0695; found: 268.0701.

N-Allyl-5-chloro-2-iodoaniline (1b)

Yield: 539 mg (77%); Colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57–7.52 (m, 1 H), 6.53–6.43 (m, 2 H), 6.01–5.88 (m, 1 H), 5.35–5.21 (m, 2 H), 4.4 (s, 1 H), 3.81 (m, *J* = 5.5, 1.7 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.9, 139.5, 135.6, 133.9, 118.6, 116.9, 110.8, 82.3, 46.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C_9H_9ClIN: 293.9541; found: 293.9547.

N-Allyl-2-iodo-5-methylaniline (1h)

Yield: 484 mg (74%); Colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.60 (d, *J* = 7.9 Hz, 1 H), 6.47 (d, *J* = 2.0 Hz, 1 H), 6.40–6.36 (m, 1 H), 6.04 (m, *J* = 17.2, 10.3, 5.1 Hz, 1 H), 5.41–5.26 (m, 2 H), 4.34 (s, 1 H), 3.88 (d, *J* = 5.2 Hz, 2 H), 2.35 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.8, 139.4, 138.6, 134.7, 119.9, 116.4, 111.8, 81.7, 46.6, 21.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{12}IN$: 274.0087; found: 274.0093.

***N*-(2-Bromoallyl)-2-iodoaniline (1j)**

Yield: 419 mg (52%); Colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75–7.65 (m, 1 H), 7.26–7.17 (m, 1 H), 6.59–6.49 (m, 2 H), 5.84 (q, *J* = 1.8 Hz, 1 H), 5.60 (q, *J* = 1.9 Hz, 1 H), 4.77 (s, 1 H), 4.08 (d, *J* = 4.3 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.8, 139.2, 130.1, 129.5, 119.7, 116.8, 111.1, 85.4, 52.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C_9H_9IBrN: 337.9036; found: 337.9041.

***N*-Allyl-5-fluoro-2-iodoaniline (1g)**

Yield: 423 mg (64%); Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60–7.54 (m, 1 H), 6.32–6.20 (m, 2 H), 6.00–5.89 (m, 1 H), 5.35–5.21 (m, 2 H), 4.45 (s, 1 H), 3.81 (m, *J* = 5.5, 1.7 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.5 (d, *J* = 181.5 Hz), 148.6 (d, *J* = 9.0 Hz), 139.4 (d, *J* = 7.5 Hz), 134.0, 116.9, 105.6 (d, *J* = 17.3 Hz), 98.5 (d, *J* = 20.2 Hz), 77.9 (d, *J* = 2.2 Hz), 46.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –112.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C_9H_9IFN: 277.9836; found: 277.9842.

Benzothiazole Derivatives 3; General Procedure

In a Schlenk tube, **1** or **2** (0.5 mmol), and K_2S (2.2 equiv) and were added and the tube was charged with argon three times. DMF (2.0 mL) was then added and the mixture was stirred at 130 °C for 12 hours. After the mixture was cooled to r.t., the reaction was quenched with H_2O (15 mL) and the mixture was extracted with EtOAc (3 × 15 mL). The combined organic layer was dried ($MgSO_4$), filtered and evaporated followed by a silica gel column chromatography (EtOAc/PE = 1:100) to afford product **3**.

Ethylbenzo[*d*]thiazole (3a)

Yield: 44 mg (54%); 36 mg (43%); brown oil.

IR (neat): 1519, 1455, 1434, 1309, 1277, 1238, 1124, 946, 755, 727, 706 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01–7.92 (m, 1 H), 7.87–7.79 (m, 1 H), 7.48–7.39 (m, 1 H), 7.39–7.30 (m, 1 H), 3.15 (q, *J* = 7.6 Hz, 2 H), 1.47 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.7, 153.4, 135.2, 126.0, 124.7, 122.6, 121.6, 27.9, 13.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C_9H_9NS: 164.0528; found: 164.0531.

6-Chloro-2-ethylbenzo[*d*]thiazole (3b)

Yield: 44 mg (45%); 71 mg (72%); brown solid; mp 45–46 °C.

IR (neat): 1616, 1592, 1519, 1480, 1436, 1397, 1299, 1268, 1168, 1049, 857, 813, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87–7.83 (m, 1 H), 7.80–7.77 (m, 1 H), 7.42–7.36 (m, 1 H), 3.16–3.09 (m, 2 H), 1.45 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz,$CDCl_3$): δ = 174.2, 151.9, 136.4, 130.6, 126.8, 123.3, 121.2, 27.9, 13.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C_9H_8NSCl: 198.0139; found: 198.0137.

2-Ethyl-6-fluorobenzo[*d*]thiazole (3c)

Yield: 38 mg (42%); 68 mg (76%); brown oil.

IR (neat): 1606, 1567, 1527, 1455, 1248, 1196, 1046, 911, 846, 812, 593 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95–7.83 (m, 1 H), 7.57–7.48 (m, 1 H), 7.22–7.13 (m, 1 H), 3.12 (q, *J* = 7.6 Hz, 2 H), 1.46 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.3 (d, *J* = 4.3 Hz), 160.3 (d, *J* = 243.5 Hz), 150.0, 136.1 (d, *J* = 12.6 Hz), 123.4 (d, *J* = 9.4 Hz), 114.5 (d, *J* = 24.4 Hz), 107.9 (d, *J* = 27.5 Hz), 27.9, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –117.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C_9H_8NSF: 182.0434; found: 182.0436.

Ethyl-6-(trifluoromethyl)benzo[*d*]thiazole (3d)

Yield: 53 mg (46%); 52 mg (45%); yellow oil.

IR (neat): 1581, 1415, 1315, 1275, 1161, 1115, 1081, 1048, 881, 826, 720, 646 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16–8.10 (m, 1 H), 8.07–8.00 (m, 1 H), 7.73–7.65 (m, 1 H), 3.18 (q, *J* = 7.6 Hz, 2 H), 1.48 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.1, 155.4, 135.3, 127.1 (q, *J* = 32.3 Hz), 124.4 (q, *J* = 270.8 Hz), 123.1 (d, *J* = 38.0 Hz), 123.0, 119.3 (d, *J* = 23.0 Hz), 28.1, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –61.35.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{10}H_8NSF_3$: 232.0402; found: 232.0405.

Ethyl-6-methylbenzo[*d*]thiazole (3e)

Yield: 34 mg (38%); 36 mg (41%); yellow oil.

IR (neat): 1605, 1523, 1457, 1377, 1304, 1277, 1165, 1054, 948, 811, 586 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87–7.81 (m, 1 H), 7.65–7.61 (m, 1 H), 7.28–7.23 (m, 1 H), 3.12 (q, *J* = 7.6 Hz, 2 H), 2.47 (s, 3 H), 1.46 (td, *J* = 7.6, 0.7 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.6, 151.5, 135.3, 134.7, 127.5, 122.1, 121.4, 27.8, 21.5, 13.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{11}NS$: 178.0685; found: 178.0681.

5-Chloro-2-ethylbenzo[*d*]thiazole (3f)

Yield: 60 mg (61%); brown solid; mp 46–47 °C.

IR (neat): 1724, 1658, 1579, 1503, 1453, 1435, 1284, 1174, 1070, 948, 902, 797, 769, 731, 631 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 2.0 Hz, 1 H), 7.74 (d, *J* = 8.5 Hz, 1 H), 7.32 (dd, *J* = 8.5, 2.0 Hz, 1 H), 3.14 (q, *J* = 7.6 Hz, 2 H), 1.46 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.7, 154.3, 133.5, 132.0, 125.2, 122.6, 122.3, 28.0, 13.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C_9H_8NSCl: 198.0139; found: 198.0145.

2-Ethyl-5-fluorobenzo[*d*]thiazole (3g)

Yield: 60 mg (66%); 39 mg (43%); yellow oil.

IR (neat): 1606, 1567, 1515, 1454, 1308, 1266, 1147, 1123, 1049, 957, 856, 797, 693, 624 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79–7.71 (m, 1 H), 7.67–7.60 (m, 1 H), 7.16–7.08 (m, 1 H), 3.14 (q, *J* = 7.6 Hz, 2 H), 1.46 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.4, 161.8 (d, *J* = 59.4 Hz), 154.3 (d, *J* = 11.3 Hz), 129.3 (d, *J* = 10.3 Hz), 122.2 (d, *J* = 10.2 Hz), 113.4 (d, *J* = 25.4 Hz), 108.9 (d, *J* = 2.5 Hz), 28.0, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –116.4.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C_9H_8NSF: 182.0434; found: 182.0436.

2-Ethyl-5-methylbenzo[*d*]thiazole (3h)

Yield: 45 mg (51%); yellow oil.

IR (neat): 1728, 1607, 1518, 1455, 1305, 1155, 1063, 1002, 947, 827, 795, 611.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80–7.74 (m, 1 H), 7.72–7.66 (m, 1 H), 7.19–7.12 (m, 1 H), 3.12 (q, *J* = 7.6 Hz, 2 H), 2.48 (s, 3 H), 1.45 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.7, 153.8, 136.0, 132.05, 126.3, 122.6, 121.1, 27.9, 21.5, 13.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{11}NS$: 178.0685; found: 178.0685.

2-Phenethylbenzo[*d*]thiazole (3k)

Yield: 30 mg (25%); yellow oil.

IR (neat):1602, 1519, 1454, 1435, 1312, 1243, 1189, 1062, 1014, 758, 729, 699 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11–7.97 (m, 1 H), 7.91–7.84 (m, 1 H), 7.52–7.46 (m, 1 H), 7.42–7.38 (m, 1 H), 7.38–7.27 (m, 5 H), 3.47 (dd, *J* = 9.2, 6.9 Hz, 2 H), 3.25 (dd, *J* = 9.4, 6.7 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 153.3, 140.3, 135.3, 128.7, 128.6, 126.6, 126.1, 124.9, 122.7, 121.7, 36.1, 35.7.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{13}NS$: 262.0661; found: 262.0664.

2-Propylbenzo[*d*]thiazole (3m)

Yield: 39 mg (44%); yellow oil.

IR (neat): 1518, 1455, 1434, 1310, 1278, 1243, 1153, 1059, 1011, 756, 727 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00–7.94 (m, 1 H), 7.86–7.80 (m, 1 H), 7.48–7.42 (m, 1 H), 7.37–7.31 (m, 1 H), 3.12–3.05 (m, 2 H), 1.95–1.87 (m, 2 H), 1.05 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.3, 153.4, 135.3, 126.0, 124.7, 122.6, 121.6, 36.4, 23.2, 13.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{11}NS$: 178.0685; found: 178.0684.

5-Bromo-2-ethylbenzo[*d*]thiazole (3n)

Yield: 99 mg (81%); brown solid; mp 45–46 °C.

IR (neat): 1575, 1593, 1501, 1451, 1432, 1405, 1298, 1255, 1173, 1052, 950, 890, 795, 628, 603 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13–8.08 (m, 1 H), 7.70–7.64 (m, 1 H), 7.46–7.41 (m, 1 H), 3.17–3.10 (m, 2 H), 1.45 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.5, 154.6, 134.0, 127.8, 125.5, 122.6, 119.5, 27.9, 13.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C_9H_8NSBr: 241.9634; found: 241.9633.

(*tert*-Butyl)-2-ethylbenzo[*d*]thiazole (3o)

Yield: 46 mg (42%); brown oil.

IR (neat): 1727, 1574, 1517, 1455, 1396, 1377, 1313, 1275, 1170, 1072, 1045, 963, 780, 726 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91–7.86 (m, 1 H), 7.84–7.81 (m, 1 H), 7.53–7.48 (m, 1 H), 3.12 (q, *J* = 7.6 Hz, 2 H), 1.45 (t, *J* = 7.6 Hz, 3 H), 1.38 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.0, 151.3, 148.1, 135.2, 124.1, 121.9, 117.7, 35.0, 31.7, 27.8, 14.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{17}NS$: 220.1154; found: 220.1142.

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Supporting Information

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