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SILVER-MEDIATED 2-ARYLATION/ALKYLATION/ACYLATION OF BENZOTHIAZOLES WITH ALDEHYDES IN WATER

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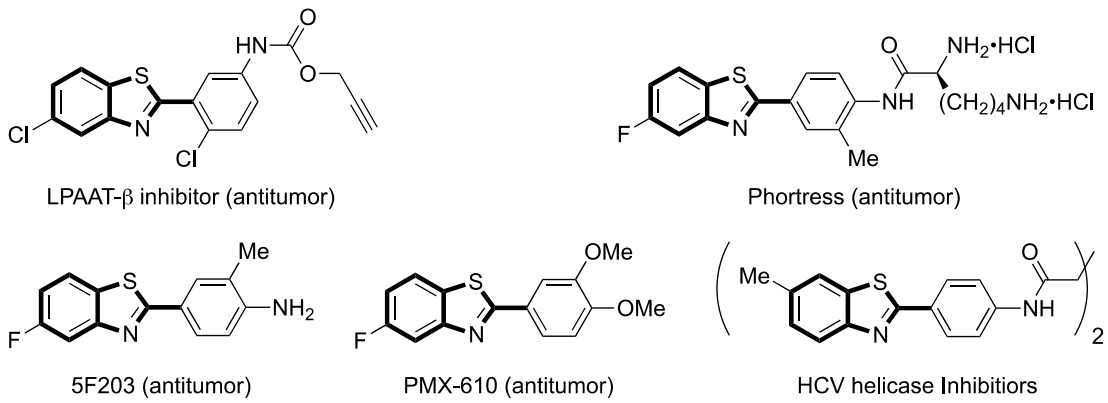
Abstract – An efficient and environmentally benign method was developed for the facile synthesis of various 2-aryl and 2-alkyl substituted benzothiazoles in moderate to good yields, using a silver-mediated redox condensation of benzothiazoles and aldehydes in water. Furthermore, this method is also applicable to prepare 2-acyl benzothiazoles.

INTRODUCTION

2-Substituted benzothiazoles are important building blocks of pharmaceuticals and natural products.[1] For instance, the antitumor and anti-hepatitis C virus (anti-HCV) drug molecules contain benzothiazole moieties (Scheme 1).[2] Therefore, the development of efficient methods for the synthesis of 2-substituted benzothiazoles and its analogues has drawn much attention.



Scheme 1. Some Drugs Contain 2-Substituted Benzothiazole

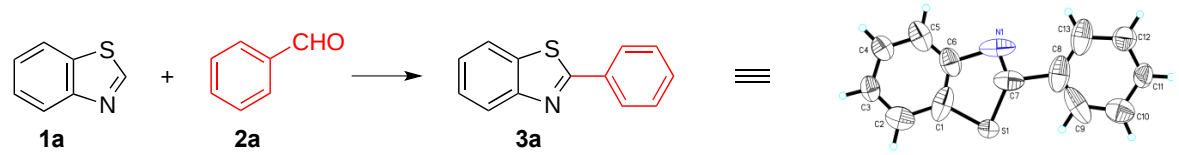
To date, some synthetic routes have been developed for the preparation of 2-substituted benzothiazoles. It can be divided into three broad categories: (1) the condensation of 2-aminothiophenols with aryl aldehydes, carboxylic acids, nitriles, acyl chlorides, or alcohols;[3] (2) transition metal-catalyzed direct C–H activation and C–C coupling of benzothiazole with aryl halides, arylboronic acids, iodobenzenediacetate, arenediazonium salts, aryl sulfamates, aryltrimethylammonium triflates, arene benzenesulfonyl chlorides, substituted benzoic acids, or triarylbismuth reagents;[4] (3) redox condensation of benzothiazoles with aldehydes, benzylic alcohols, and styrenes.[5] However, there are some drawbacks in the above methods. For example, the expensive and unstable 2-aminothiophenol was used as starting materials; expensive transition metal was used as catalysts. To continue our interest in silver catalysis,[6] we report herein a silver-mediated redox condensation of benzothiazoles with aromatic and aliphatic aldehydes, as well as phenylglyoxal in water, affording a variety of 2-aryl, 2-alkyl, and 2-acyl substituted benzothiazoles in high yields.

RESULTS AND DISCUSSION

Initially, the redox condensation of benzothiazole (**1a**) and benzaldehyde (**2a**) in AcOH-H_2O (8:2) at 100 °C for 24 h under air was chosen as a model reaction. As shown in Table 1, the different oxidants such as AgOTf, $AgNO_3$, Ag_2CO_3, AgOTs, DTBP, $Cu(OAc)_2$, and O_2 were investigated (entries 1–7). And the highest yield of **3a** (88%) was obtained using AgOTs as an oxidant. However, the yield of **3a** was decreased with the decrease of the amount of oxidant (entries 8–9). Interestingly, up to 90% yield was obtained when the reaction was performed under nitrogen atmosphere (entry 10). It maybe ascribe to the oxidation of the benzaldehyde to benzoic acid under air.[7] It was found that there is no effect on the yield even if shortening the reaction time to 12 h (entries 10–12). Next, the ratio of AcOH and H_2O was examined (entries 13–15). An 81% yield of **3a** was obtained in an equal volume of AcOH and H_2O (entry 13). To our delight, **3a** was isolated with 95% yield in H_2O (entry 15). And then, the reaction was also conducted at lower temperature, but the yield decreased apparently (entries 16–17). The structure of **3a** was determined not only by ^1H NMR, ^{13}C NMR, and HRMS, but also by single crystal X-ray analysis (CCDC 1814089).

With the optimized reaction conditions in hand, the substrate scope was investigated. As shown in Scheme 2, the reaction of benzothiazole (**1a**) with both electron-poor and electron-rich aromatic aldehydes was conducted smoothly, giving the corresponding products **3b**–**3n** in 46–95% yield. Notably, the aldehydes bearing a free hydroxyl group or methylal moiety were also tolerated, providing the desired products **3m** and **3n** in 46% and 63% yields, respectively. In addition, the 1-naphthaldehyde (**2o**) and furan-2-carbaldehyde (**2p**) were also applicable to this reaction, and the desired benzothiazoles **3o** and **3p** were obtained in 87% and 79% yields, respectively. To our delighted, the aliphatic aldehydes like

Table 1. Optimization of the Reaction Conditions[a]



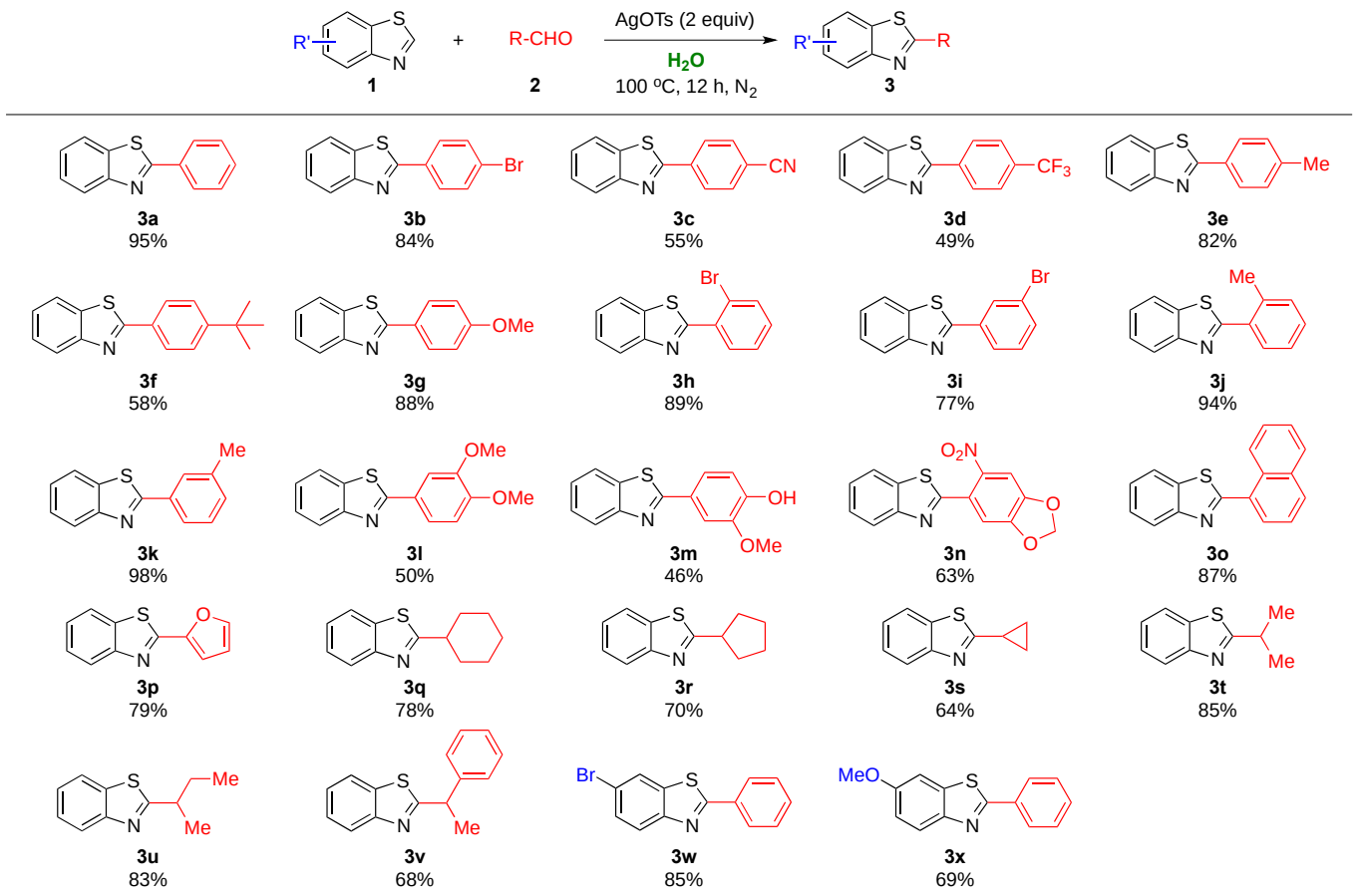
Entry	Oxidant (equiv)	Solvent (V:V)	T (°C)	t (h)	Yield (%)[b]
1	AgOTf (2)	AcOH-H_2O (8:2)	100	24	64
2	$AgNO_3$ (2)	AcOH-H_2O (8:2)	100	24	12
3	Ag_2CO_3 (2)	AcOH-H_2O (8:2)	100	24	33
4	AgOTs (2)	AcOH-H_2O (8:2)	100	24	88
5	DTBP (2)	AcOH-H_2O (8:2)	100	24	12
6	$Cu(OAc)_2$ (2)	AcOH-H_2O (8:2)	100	24	20
7	O_2 (1atm)	AcOH-H_2O (8:2)	100	24	9
8	AgOTs (1.5)	AcOH-H_2O (8:2)	100	24	77
9	AgOTs (1)	AcOH-H_2O (8:2)	100	24	46
10[c]	AgOTs (2)	AcOH-H_2O (8:2)	100	24	90
11[c]	AgOTs (2)	AcOH-H_2O (8:2)	100	12	90
12[c]	AgOTs (2)	AcOH-H_2O (8:2)	100	9	86
13[c]	AgOTs (2)	AcOH-H_2O (5:5)	100	12	81
14[c]	AgOTs (2)	AcOH	100	12	17
15[c]	**AgOTs (2)**	**H_2O**	**100**	**12**	**95**
16[c]	AgOTs (2)	H_2O	90	12	72
17[c]	AgOTs (2)	H_2O	80	12	52

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), oxidant, solvent (2 mL), under air. DTBP: di-*t*-butyl peroxide. [b]Isolated yield. [c]Under nitrogen atmosphere.

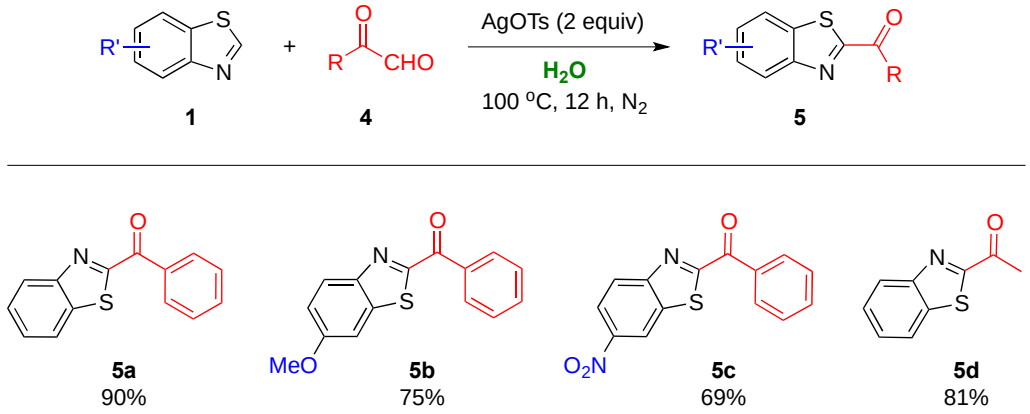
cyclohexanecarbaldehyde (**2q**), cyclopentanecarbaldehyde (**2r**), cyclopropanecarbaldehyde (**2s**), isobutyraldehyde (**2t**), 2-methylbutanal (**2u**), as well as 2-phenylpropanal (**2v**) are also applicable, and the corresponding products **3q**–**3v** were obtained in 64–85% yield. Subsequently, the scope of benzothiazoles was also examined. For example, the electron-poor 6-bromobenzothiazole and electron-rich 6-methoxybenzothiazole gave the desired product **3w** and **3x** in 85% and 69% yields, respectively.

Aryl heteroaryl ketones are important skeletons of pharmaceuticals, such as diflumidone, raloxifene and tiaprofenic acid.[8] Liu and Wang reported the redox condensation of benzothiazoles with phenylglyoxal, and 2-benzoylbenzothiazole was obtained with only 31% and 44% yields.[9] To further demonstrate the scope of this methodology, the phenylglyoxal **4a** and methylglyoxal **4b** were also subjected to the

reaction with benzothiazoles (Scheme 3). To our delighted, the corresponding 2-benzoylbenzothiazoles **5a**–**5c** and 2-acetylbenzothiazole **5d** were obtained in 69–90% yields.

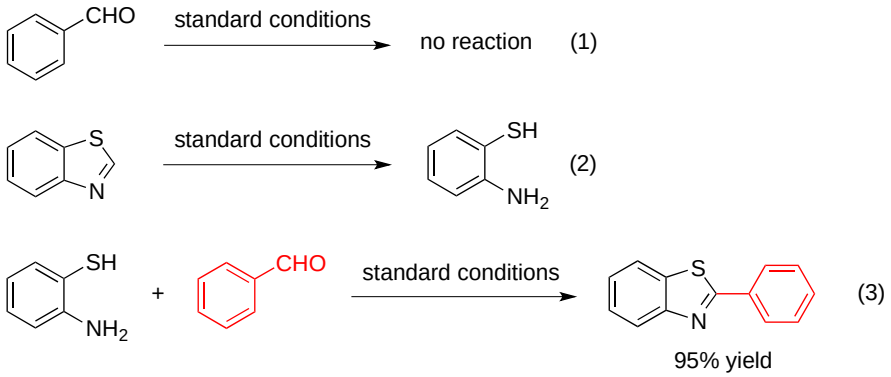


Scheme 2. Substrate scope. Reaction conditions: **1** (0.5 mmol), **2** (0.6 mmol), AgOTs (2 equiv), H_2O (2 mL), 12 h, 100 °C, under N_2 atmosphere, isolated yield.



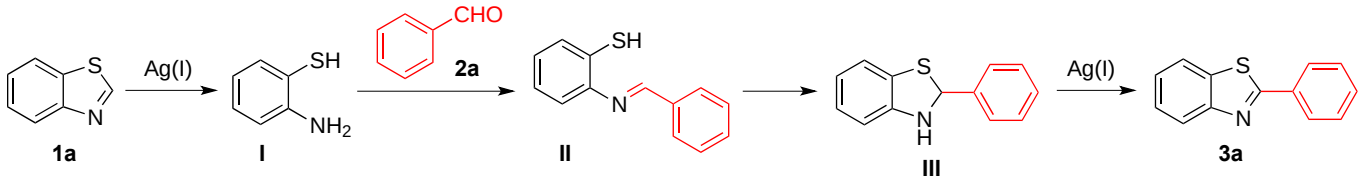
Scheme 3. Synthesis of 2-Acylbenzothiazoles. Reaction conditions: **1** (0.5 mmol), **4** (0.6 mmol), AgOTs (2 equiv), H_2O (2 mL), 12 h, 100 °C, under N_2 atmosphere, isolated yield.

To understand the reaction pathway, several control experiments were performed. As shown in Scheme 4, under the standard conditions, the benzaldehyde remained intact (eq. 1), whereas benzothiazole was completely consumed to give 2-aminothiophenol quantitatively (eq. 2). The reaction of benzaldehyde and 2-amino thiophenol proceeded smoothly to give the desired product in 95% yield (eq. 3).



Scheme 4. Control Experiments. Standard conditions: AgOTs (2 equiv), H_2O (2 mL), 12 h, 100 °C, under N_2 atmosphere.

Based on the results of control experiments and previous reports,[5b,5c,5f,10] a possible reaction pathway was proposed as shown in Scheme 5. Initially, the benzothiazole (**1a**) will be opened to give 2-aminobenzenethiol **I** by silver salt. And then, the condensation of intermediate **I** with benzaldehyde (**2a**) will generate imine **II**. Next, the intramolecular cyclization of imine **II** will produce **III**, followed by oxidation to give the desired product **3a**.



Scheme 5. A Possible Reaction Pathway

In summary, we have developed an efficient method for the synthesis of 2-aryl, 2-aklyl, and 2-acyl-benzothiazoles from readily availably benzothiazoles and corresponding aldehydes in the presence of silver salt with water as green solvent. Further studies on the detail mechanism and the scope of other heteroaromatics like benzoimidazoles, benzoxazoles are underway in our laboratory.

EXPERIMENTAL

Unless otherwise noted, all the reagents, catalysts and solvents were purchased from commercial suppliers and used without further purification. Column Chromatography was performed with silica gel

(200–300 mesh). NMR spectra were recorded on Bruker AVANCE III (400 MHz) spectrometers. $CDCl_3$ was used as solvent for the NMR analysis with tetramethylsilane as the internal standard. Chemical shifts were reported upfield to TMS (0.00 ppm) for ^1H NMR and relative to $CDCl_3$ (77.0 ppm) for ^{13}C NMR. HRMS spectra were acquired using an Agilent 6210 ESI/TOF mass spectrometer. Compounds **3a** were collected at 100 K on a Rigaku Oxford Diffraction Supernova Dual Source, Cu at Zero equipped with an AtlasS2 CCD using Cu Kα radiation.

General procedure for the synthesis of products

A sealed pressure vessel was charged with benzothiazole (68 mg, 0.5 mmol), AgOTs (280 mg, 1 mmol), aldehyde (0.6 mmol) and 2.0 mL of H_2O. The resulting solution was stirred at 100 ºC for 12 h under N_2. Upon completion of the reaction, H_2O (8.0 mL) was added, then extracted with EtOAc (5 mL × 3), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was further purified with flash column chromatography.

2-Phenylbenzothiazole (3a) (CAS No.: 883-93-2)

Following general procedure gave product **3a** as a white solid. 95% yield; mp 111–113 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16-8.11 (m, 3H), 7.96 (d, J = 7.6 Hz, 1H), 7.57-7.52 (m, 4H), 7.44 (td, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 154.2, 135.1, 133.7, 131.0, 129.0, 127.6, 126.3, 125.2, 123.3, 121.6 ppm; HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{13}H_{10}NS$ 212.0528, found 212.0526.

2-(4-Bromophenyl)benzothiazole (3b) (CAS No.: 19654-19-4)

Following general procedure gave product **3b** as a white solid. 84% yield; mp 132–134 ºC. ^1H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 8.0 Hz, 1H), 8.02 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 2H), 7.95 (d, J = 8.0 Hz, 1H), 7.67 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 2H), 7.55 (t, J = 7.6 Hz, 1H), 7.45 (t, J = 7.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 154.1, 135.1, 132.6, 132.3, 128.9, 126.5, 125.5, 125.4, 123.3, 121.7 ppm.

2-(4-Cyanophenyl)benzothiazole (3c) (CAS No.: 17930-02-8)

Following general procedure gave product **3c** as a white solid. 55% yield; mp 165–166 ºC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 8.4 Hz, 2H), 8.16 (d, J = 8.4 Hz, 1H), 7.99 (d, J = 7.6 Hz, 1H), 7.84 (d, J = 8.4 Hz, 2H), 7.59 (t, J = 7.6 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 154.0, 137.5, 135.3, 132.8, 128.0, 126.9, 126.1, 123.8, 121.8, 118.3, 114.2 ppm.

2-(4-Trifluoromethylphenyl)benzothiazole (3d) (CAS No.: 134384-31-9)

Following general procedure gave product **3d** as a white solid. 49% yield; mp 159–161 ºC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 8.0 Hz, 2H), 8.16 (d, J = 8.0 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 8.4 Hz, 2H), 7.58 (t, J = 7.6 Hz, 1H), 7.48 (t, J = 7.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 154.1, 136.8, 135.2, 132.7, 132.3, 127.8, 126.7, 126.0 (m), 123.7, 122.5, 121.8 ppm.

2-(4-Methylphenyl)benzothiazole (3e) (CAS No.: 16112-21-3)

Following general procedure gave product **3e** as a white solid. 82% yield; mp 85–86 ºC; ^1H NMR (400

MHz, $CDCl_3$) δ 8.11 (d, J = 8.0 Hz, 1H), 8.03 (d, J = 8.4 Hz, 2H), 7.94 (d, J = 7.6 Hz, 1H), 7.53 (td, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H), 7.42 (td, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1H), 7.35 (d, J = 8.0 Hz, 2H), 2.47 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 154.2, 141.5, 135.0, 131.0, 129.7, 127.5, 126.3, 125.0, 123.1, 121.6, 21.6 ppm.

2-(4-(*tert*-Butyl)phenyl)benzothiazole (3f) (CAS No.: 56048-52-3)

Following general procedure gave product **3f** as a red solid. 58% yield; mp 108–109 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 8.4 Hz, 1H), 8.08 (d, J = 8.4 Hz, 2H), 7.95 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 8.4 Hz, 2H), 7.53 (d, J = 7.2 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 1.42 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 154.6, 154.2, 135.0, 130.9, 127.4, 126.2, 126.0, 125.0, 123.1, 121.6, 35.0, 31.2 ppm.

2-(4-Methoxyphenyl)benzothiazole (3g) (CAS No.: 6265-92-5)

Following general procedure gave product **3g** as a green solid. 88% yield; mp 123–124 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.4 Hz, 3H), 7.93 (d, J = 7.6 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.05 (d, J = 8.4 Hz, 2H), 3.93 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 162.0, 154.2, 134.9, 129.2, 126.4, 126.2, 124.8, 122.9, 121.5, 114.4, 55.5 ppm.

2-(2-Bromophenyl)benzothiazole (3h) (CAS No.: 22901-00-4)

Following general procedure gave product **3h** as a yellow solid. 89% yield; mp 68–69 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 8.4 Hz, 1H), 8.05 (dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.58 (td, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H), 7.49 (td, J_1 = 7.6 Hz, J_2 = 3.2 Hz, 2H), 7.37 (td, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 152.8, 136.2, 134.5, 134.1, 132.2, 131.3, 127.6, 126.3, 125.5, 123.6, 122.1, 121.5 ppm.

2-(3-Bromophenyl)benzothiazole (3i) (CAS No.: 19654-14-9)

Following general procedure gave product **3i** as a white solid. 77% yield; mp 120–121 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (t, J = 1.6 Hz, 1H), 8.12 (d, J = 8.0 Hz, 1H), 8.04 (d, J = 7.6 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.56 (t, J = 7.6 Hz, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.41 (t, J = 8.0 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 154.0, 135.5, 135.1, 133.8, 130.5, 130.3, 126.6, 126.2, 125.6, 123.5, 123.2, 121.7 ppm.

2-(2-Methylphenyl)benzothiazole (3j) (CAS No.: 15903-58-9)

Following general procedure gave product **3j** as a white solid. 94% yield; mp 56–57 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.4 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 7.6 Hz, 1H), 7.56 (t, J = 7.2 Hz, 1H), 7.48-7.35 (s, 4H), 2.72 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 153.8, 137.3, 135.6, 133.1, 131.6, 130.6, 130.0, 126.2, 126.1, 125.1, 123.4, 121.4, 21.4 ppm.

2-(3-Methylphenyl)benzothiazole (3k) (CAS No.: 1211-32-1)

Following general procedure gave product **3k** as a white solid. 98% yield; mp 67–68 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.4 Hz, 1H), 8.00 (s, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.93 (d, J = 7.6 Hz, 1H),

7.54 (td, J_1 = 7.2 Hz, J_2 = 1.6 Hz, 1H), 7.43 (td, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 2H), 7.36 (d, J = 7.6 Hz, 1H), 2.53 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 154.1, 138.9, 135.1, 133.5, 131.9, 129.0, 128.0, 126.3, 125.2, 124.9, 123.2, 121.6, 21.4 ppm.

2-(3,4-Dimethoxyphenyl)benzothiazole (3l) (CAS No.: 6638-45-5)

Following general procedure gave product **3l** as a white solid. 50% yield; mp 130–131 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 2.4 Hz, 1H), 7.65 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1H), 7.53 (td, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 1H), 7.42 (td, J_1 = 7.2 Hz, J_2 = 0.8 Hz, 1H), 6.99 (d, J = 8.4 Hz, 1H), 4.07 (s, 3H), 4.01 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 154.1, 151.6, 149.3, 134.9, 126.7, 126.3, 124.9, 122.9, 121.5, 121.2, 111.0, 109.8, 56.2, 56.1 ppm.

2-(4-Hydroxy-3-methoxyphenyl)benzothiazole (3m) (CAS No.: 36341-25-0)

Following general procedure gave product **3m** as a white solid. 46% yield; mp 166–168 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.77 (d, J = 2.0 Hz, 1H), 7.61 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1H), 7.53 (td, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 1H), 7.42 (td, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1H), 7.06 (d, J = 8.4 Hz, 1H), 6.00 (s, 1H), 4.08 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 154.1, 148.5, 146.9, 134.9, 126.3, 126.2, 124.8, 122.8, 122.0, 121.5, 114.7, 109.3, 56.3 ppm.

2-(6-Nitrobenzo[1,3]dioxol-5-yl)benzothiazole (3n)

Following general procedure gave product **3n** as a yellow solid. 63% yield; mp 146–147 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 7.2 Hz, 1H), 7.97 (d, J = 8.4 Hz, 1H), 7.57 (td, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 1H), 7.54 (s, 1H), 7.48 (td, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H), 7.16 (s, 1H), 6.25 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 153.3, 151.0, 149.3, 143.5, 136.0, 126.5, 125.8, 124.5, 123.8, 121.6, 110.7, 105.8, 103.6 ppm.

2-(Naphthalen-1-yl)benzothiazole (3o) (CAS No.: 56048-50-1)

Following general procedure gave product **3o** as a white solid. 87% yield; mp 125–126 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (d, J = 8.8 Hz, 1H), 8.24 (d, J = 8.0 Hz, 1H), 8.01-7.93 (m, 4H), 7.66-7.55 (m, 4H), 7.48 (td, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 154.1, 135.4, 134.0, 131.0, 130.8, 130.6, 129.3, 128.4, 127.6, 126.5, 126.2, 125.8, 125.2, 124.9, 123.5, 121.3 ppm.

2-(Furan-2-yl)-1,3-benzothiazole (3p) (CAS No.: 1569-98-8)

Following general procedure gave product **3p** as a gray solid. 79% yield; mp 90–91 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.0 Hz, 1H), 7.94 (dd, J_1 = 8.0 Hz, J_2 = 0.4 Hz, 1H), 7.65 (dd, J_1 = 1.6 Hz, J_2 = 0.8 Hz, 1H), 7.53 (td, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H), 7.42 (td, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 7.24 (dd, J_1 = 3.2 Hz, J_2 = 0.8 Hz, 1H), 6.64 (dd, J_1 = 3.6 Hz, J_2 = 2.0 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 153.8, 148.8, 144.7, 134.3, 126.5, 125.2, 123.1, 121.6, 112.6, 111.5 ppm.

2-Cyclohexylbenzothiazole (3q) (CAS No.: 40115-03-5)

Following general procedure gave product **3q** as a yellow oil. 78% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ

8.02 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 7.88 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 7.48 (t, J = 8.4 Hz, 1H), 7.36 (t, J_1 = 8.4 Hz, 1H), 3.17-3.11 (m, 1H), 2.27-2.21 (m, 2H), 1.95-1.89 (m, 2H), 1.73-1.63 (m, 2H), 1.54-1.30 (m, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.6, 153.1, 134.6, 125.8, 124.5, 122.6, 121.6, 43.5, 33.5, 26.1, 25.8 ppm.

2-Cyclopentylbenzothiazole (3r) (CAS No.: 40115-02-4)

Following general procedure gave product **3r** as a yellow oil. 70% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.0 Hz, 1H), 7.88 (dd, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1H), 7.48 (td, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H), 7.37 (td, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H), 3.62-3.57 (m, 1H), 2.30-2.00 (m, 2H), 1.99-1.87 (m, 4H), 1.80-1.77 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 153.2, 134.8, 125.8, 124.5, 122.5, 121.5, 44.8, 34.1, 25.6 ppm.

2-Cyclopropylbenzothiazole (3s) (CAS No.: 1248473-57-5)

Following general procedure gave product **3s** as a yellow oil. 64% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.46 (td, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 1H), 7.35 (td, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 2.48-2.41 (m, 1H), 1.30-1.26 (m, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 153.4, 134.1, 125.9, 124.3, 122.1, 121.4, 15.3, 11.7 ppm.

2-Isopropyl-1,3-benzothiazole (3t) (CAS No.: 17626-86-7)

Following general procedure gave product **3t** as a yellow oil. 85% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.4 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.48 (td, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H), 7.37 (td, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H), 3.52-3.41 (m, 1H), 1.51 (d, J = 6.8 Hz, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.6, 153.2, 134.7, 125.9, 124.6, 122.6, 121.6, 34.1, 23.0 ppm.

2-(1-Methylpropyl)-2-benzothiazole (3u) (CAS No.: 17626-87-8)

Following general procedure gave product **3u** as a pale yellow oil. 83% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.0 Hz, 1H), 8.89 (d, J = 8.0 Hz, 1H), 7.48 (td, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H), 7.37 (td, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 3.30-3.21 (m, 1H), 2.01-1.90 (m, 1H), 1.87-1.78 (m, 1H), 1.50 (d, J = 6.8 Hz, 3H), 1.02 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.9, 153.1, 134.7, 125.8, 124.6, 122.6, 121.6, 41.1, 30.7, 20.8, 11.9 ppm.

1-Methyl-2-(1-phenylethyl)benzothiazole (3v) (CAS No.: 111259-61-1)

Following general procedure gave product **3v** as a white solid. 68% yield; mp 34–36 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.52-7.33 (m, 7H), 4.65 (q, J = 7.6 Hz, 1H), 1.93 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 153.2, 143.2, 135.4, 128.8, 127.7, 127.3, 125.9, 124.8, 122.9, 121.5, 44.9, 21.3 ppm.

6-Bromo-2-phenylbenzothiazole (3w) (CAS No.: 77333-67-6)

Following general procedure gave product **3w** as a yellow solid. 85% yield; mp 149–150 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13-8.09 (m, 3H), 7.97 (d, J = 8.8 Hz, 1H), 7.65 (dd, J_1 = 8.8 Hz, J_2 = 2.0 Hz, 1H),

7.55 (dd, J_1 = 5.2 Hz, J_2 = 2.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 153.0, 136.7, 133.2, 131.3, 129.9, 129.1, 127.6, 124.3, 124.2, 118.8 ppm.

6-Methoxy-2-phenylbenzothiazole (3x) (CAS No.: 10205-69-3)

Following general procedure gave product **3x** as a white solid. 69% yield; mp 112–113 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10-8.08 (m, 2H), 8.01 (d, J = 8.8 Hz, 1H), 7.55-7.50 (m, 3H), 7.41 (d, J = 2.8 Hz, 1H), 7.15 (dd, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 1H), 3.94 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 157.8, 148.7, 136.4, 133.8, 130.6, 129.0, 127.3, 123.7, 115.7, 104.2, 55.8 ppm.

1,3-Benzothiazol-2-yl(phenyl)methanone (5a) (CAS No.: 1629-75-0)

Following general procedure gave product **5a** as a yellow solid. 90% yield; mp 99–100 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 7.2 Hz, 2H), 8.30 (dd, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H), 8.07 (d, J = 6.8 Hz, 1H), 7.75-7.70 (m, 1H), 7.66-7.58 (m, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.4, 167.1, 153.9, 137.0, 135.0, 133.9, 131.3, 128.5, 127.7, 127.0, 125.8, 122.2 ppm.

(6-Methoxybenzothiazol-2-yl)(phenyl)methanone (5b) (CAS No.: 1443988-40-6)

Following general procedure gave product **5b** as a yellow solid. 75% yield; mp 168–170 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.46 (d, J = 8.4 Hz, 1H), 8.21 (d, J = 9.2 Hz, 1H), 8.87 (s, 1H), 7.78-7.76 (m, 1H), 7.68-7.64 (m, 2H), 7.30 (dd, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 1H), 3.92 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 185.2, 164.6, 160.1, 148.4, 139.0, 135.2, 134.4, 131.2, 129.1 126.7, 118.4, 104.9, 56.4 ppm.

(6-Nitrobenzo[d]thiazol-2-yl)(phenyl)methanone (5c) (CAS No.: 1443988-41-7)

Following general procedure gave product **5c** as a yellow solid. 69% yield; mp 159–161 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (d, J = 2.0 Hz, 1H), 8.63 (d, J = 7.2 Hz, 2H), 8.51 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1H), 8.42 (d, J = 8.4 Hz, 1H), 7.76 (t, J = 7.6 Hz, 1H), 7.64 (t, J = 8.0 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.4, 172.4, 157.2, 146.5, 137.1, 134.6, 134.2, 131.4, 128.8, 126.2, 122.1, 118.9 ppm.

1-(1,3-Benzothiazol-2-yl)ethanone (5d) (CAS No.: 1629-78-3)

Following general procedure gave product **5d** as a yellow solid. 81% yield; mp 107–109 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 7.2 Hz, 1H), 8.02 (d, J = 7.6 Hz, 1H), 7.62 (td, J_1 = 7.2 Hz, J_2 = 1.6 Hz, 1H), 7.57 (td, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 2.87 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.2, 166.5, 153.6, 137.5, 127.7, 127.0, 125.5, 122.5, 26.2 ppm.

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