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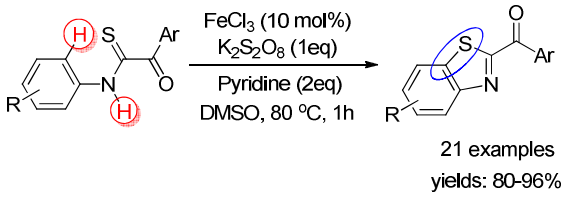
Xian Feng, Qian Wang, Zhi-Bin Huang, Da-Qing Shi *



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Fe-promoted oxidative cyclization of α-benzoylthioformanilides for synthesis of 2-benzoylbenzothiazoles

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2-Benzoylbenzothiazoles were obtained in good yields via an efficient synthesis involving oxidative cyclization of α-benzoylthioformanilides catalyzed by $FeCl_3$. This protocol has the advantages of short reaction times, moderate to good yields, convenient manipulation, and high selectivities.

Introduction

Benzothiazole derivatives are important heterocyclic compounds, and are found widely in natural products and pharmaceuticals.[1] Many compounds containing a benzothiazole motif have potent biological activities such as antibacterial, antimicrobial, anti-inflammatory, anti-HIV, antibiotic, anticancer, and antiparasitic activities.[2] Various benzothiazoles can be used as advanced materials in applications such as liquid crystals, nonlinear optics, organic light-emitting diodes, heat-resistant fibers, whitening agents, and constituents of cyanine dyes.[3] 2-Benzoylbenzothiazoles have received increasing attention recently due to the synthetic challenges and broad biological activities. It have been reported that (4-methyl-3-hydroxyphenyl)(6-hydroxy-1,3-benzothiazol-2-yl)methanone can be used as potent $cPLA_2\alpha$ inhibitors.[4] Although the synthesis of 2-arylbenzothiazoles has received much attention in the past few descades,[5] 2-benzoylbenzothiazoles have rarely been synthesized, because of the difficulty of introducing a benzoyl group at the 2-position of benzothiazoles. The methods reported for the synthesis of 2-benzoylbenzothiazoles include manganese triacetate-promoted cyclization of substituted thioformanilides,[6] condensation of 2-aminothiophenol with arylformyl aldehydes,[7] copper-catalyzed reactions of aromatic disulfide amines and aldehydes,[8] one-pot tandem reactions of 1,1-dibromoethenes with 2-aminothiophenols, promoted by $TBAF{\cdot}3H_2O$ and $RuCl_3$/air,[9] air-oxidized tandem reactions of 2-aminothiophenols and phenylacetaldehydes, catalyzed by $FeCl_3{\cdot}6H_2O$,[10] I_2-promoted domino oxidative cyclizations of aromatic ketones with *o*-aminobenzennethiols,[11] iron-catalyzed reactions of benzothiazoles and aromatic ketones, using oxygen as the oxidant,[12] iron-catalyzed aroylation of benzothiazoles with aryl ketones,[13] and CuI- and LiCl-catalyzed coupling reactions of 2-benzothiazolylizinc bromide with acid chlorides.[14] Although these methods have been successfully used to synthesize a large library of 2-benzoylbenzothiazoles, many of them suffer from drawbacks such as unsatisfactory yields, long reaction times, side reactions, expensive catalysts, and inaccessible starting materials. The development of more efficient methods for the preparation of this type of heterocyclic compound is therefore still an active research area, and there is scope for further improvements to give milder reaction conditions and improved yields.

In recent years, iron, which is an abundant, economical, and environmentally friendly metal, has shown increasing promise as a catalyst in many organic syntheses.[15] $FeCl_3$, in particular, is cheap and readily available; it is highly reactive and has been widely used as a catalyst in aza-Michael additions,[16] allylation of carbonyl compounds,[17] Nazarov cyclizations,[18] ring-opening reactions,[19] electrophilic substitutions,[20] hydroamination of alkenes,[21] Prins reactions,[22] alkylation,[23] and other reactions.[24] Recently Lei reported Fe-catalyzed oxidative C-H functionalization/C-S bond formation for the synthesis of benzothiazoles.[25] This method has the advantages of good yields, high selectivity and mild reaction conditions. In this paper, we report the efficient synthesis of 2-benzoylbenzothiazoles via intramolecular C(Ar)–H and S–H activation/C–S bond formation catalyzed by $FeCl_3$ under mild reaction conditions (Scheme 1).

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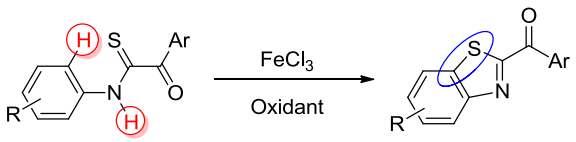


Scheme 1 Synthesis of 2-benzoylbenzothiazoles via $FeCl_3$-catalyzed C–H and S–H activation

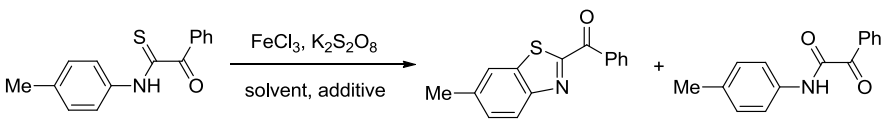
Results and discussion

We selected the oxidative reaction of *N*-(4-methyl) benzoylbenzothioamide (**1a**) as the model reaction for optimizing the reaction conditions. When the reaction was carried out using $K_2S_2O_8$ as the oxidant, in DMSO in the absence of an iron catalyst, the desired product **2a** was obtained in only 22% yield (Table 1, entry 1). When 10 mol% $FeCl_3$ was added, the yield improved to 36% (Table 1, entry 2). However, when the reaction was carried out in the presence of $FeCl_3$ without $K_2S_2O_8$, the reaction did not occur (Table 1, entry 3). The oxidant $K_2S_2O_8$ is therefore very important for this transformation. Additives were used to promote the formation of a more easily oxidized imidothiolate anion. The addition of Et_3N, Na_2CO_3, or HCl did not noticeably improve the yield (Table 1, entries 4–6). However, in the presence of pyridine, the yield of, and selectivity for, **2a** improved considerably (Table 1, entry 7). The reaction yields were similar when the reaction was performed at 120 ℃ (Table 1, entry 8) and 80 ℃. When the reaction temperature was lowered to 40 ℃, the yield decreased (Table 1, entry 9). Increasing the amounts of pyridine, $FeCl_3$, or $K_2S_2O_8$ did not improve the yield (Table 1, entries 10–12). Other solvents, namely toluene, DMF, and EtOH, were used instead of DMSO under these conditions, but changing the solvent did not affect the reaction (Table 1, entries 13–15). Based on all these experiments, the optimum reaction conditions were identified as 10 mol% $FeCl_3$, $K_2S_2O_8$ (2 equiv), and pyridine (2 equiv) in DMSO at 80 ℃

With the optimum reaction conditions in hand, we evaluated the scope and functional group compatibility of this reaction. The influence of the substituents on the aniline ring (Table 2, entries 1–7) was not a crucial factor for this transformation, and substrates bearing electron-donating groups and electron-withdrawing groups all reacted smoothly and efficiently to give **2** in moderate to excellent yields. The substituents on the benzoyl group did not affect the reaction either (Table 2, entries 8–10 and 15–21). The reaction yields were not affected by steric hindrance by either substrate. It is important that this reaction has high regioselectivity. When reactants with a *meta* substituent on the aniline ring were used, the major products were substituted at C-7 (*ortho* to the newly formed C–S bond; Table 2, entries 6, 8, and 9).

Based on literature reports,[25] we propose the following mechanism for the reaction (Scheme 2). Initially, α-benzoylthioformanilide **1** is oxidized by Fe^{3+}, and loses an electron and H^+ to form the thioyl radical intermediate **A**, accompanied by Fe^{3+} reduction to Fe^{2+}. Fe^{2+} is re-oxidized by $K_2S_2O_8$ to regenerate Fe^{3+}. Cyclization of intermediate **A**, followed by oxidation in the presence of $K_2S_2O_8$, gives the product 2-benzoylbenzothiazole **2.**

Table 1. Optimization of reaction conditions[a]



1a **2a** **3a**

Entry	Catalyst (mol%)	Oxidant	Additive	Solvent	Temp. (℃)	Yield[b] (%)	
						2a	**3a**
1	-	$K_2S_2O_8$ (1 eq)	-	DMSO	80	22	73
2	$FeCl_3$ (10)	$K_2S_2O_8$ (1 eq)	-	DMSO	80	36	63
3	$FeCl_3$ (10)	-	-	DMSO	80	NR	
4	$FeCl_3$ (10)	$K_2S_2O_8$ (1 eq)	Et_3N (2 eq)	DMSO	80	27	0

5	$FeCl_3$ (10)	$K_2S_2O_8$ (1 eq)	Na_2CO_3 (2 eq)	DMSO	80	45	0
6	$FeCl_3$ (10)	$K_2S_2O_8$ (1 eq)	HCl (2 eq)	DMSO	80	55	4
7	**$FeCl_3$ (10)**	**$K_2S_2O_8$ (1 eq)**	**Pyridine (2 eq)**	**DMSO**	**80**	**86**	**0**
8	$FeCl_3$ (10)	$K_2S_2O_8$ (1 eq)	Pyridine (2 eq)	DMSO	120	86	0
9	$FeCl_3$ (10)	$K_2S_2O_8$ (1 eq)	Pyridine (2 eq)	DMSO	40	72	3
10	$FeCl_3$ (10)	$K_2S_2O_8$ (2 eq)	Pyridine (2 eq)	DMSO	80	87	0
11	$FeCl_3$ (15)	$K_2S_2O_8$ (1 eq)	Pyridine (2 eq)	DMSO	80	87	8
12	$FeCl_3$ (10)	$K_2S_2O_8$ (1 eq)	Pyridine (4 eq)	DMSO	80	84	7
13	$FeCl_3$ (10)	$K_2S_2O_8$ (1 eq)	Pyridine (2 eq)	Toluene	80	31	7
14	$FeCl_3$ (10)	$K_2S_2O_8$ (1 eq)	Pyridine (2 eq)	EtOH	80	NR	
15	$FeCl_3$ (10)	$K_2S_2O_8$ (1 eq)	Pyridine (2 eq)	DMF	80	NR	

[a]All reactions are lead under a nitrogen atmosphere. [b]Yields were determined by LC-MS.

Conclusions

In summary, we developed an efficient protocol for the preparation of 2-benzoylbenzothiazole derivatives via C–H functionalization/C–S bond formation, catalyzed by $FeCl_3$. This protocol has the advantages of short reaction times, good yields, mild reaction conditions, high selectivities, and convenient manipulation. This novel protocol will be valuable in the construction of such heterocycles, which are of biological and medicinal interest.

Experimental section

Melting points were determined using an XT-5 melting point apparatus and are uncorrected. IR spectra were recorded (cm^{-1}) with a Varian F-1000 spectrometer, using KBr. ^1H NMR (400 or 300 MHz) and ^{13}C NMR (100 or 75 MHz) spectra were recorded using a Varian Inova-300 MHz and Varian Inova-400 MHz spectrometer, respectively, in DMSO-d_6 or $CDCl_3$ solution. *J* values are in hertz. Chemical shifts are expressed in parts per million downfield from TMS as an internal standard. HRMS of all the compounds were obtained using a Bruker MicrOTOF-QII mass spectrometer with an ESI resource. DMSO was dried and distilled from calcium hydride. Toluene was dried and distilled from sodium. All chemicals and solvents were used without further purification, unless otherwise stated. Compounds **1** were synthesized according to the procedure reported in the literature.[26]

General procedure

A Schlenk tube equipped with a stirring-bar was charged with $FeCl_3$ (0.05 mmol), α-benzoylthioformanilides 1 (0.50 mmol), and $K_2S_2O_8$ (134.9 mg, 0.50 mmol). The reaction tube was purged with nitrogen, and then pyridine (1.0 mmol) and DMSO (2 mL) were added to the reaction tube via a syringe. The Schlenk tube was warmed to 80 ℃ and stirred for 1 h. The reaction mixture was then quenched with water and extracted with ethyl acetate (20 mL × 2). The organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude products were purified by recrystallization from 95% EtOH to give pure 2 in 80–96% yields. The products were further identified using FTIR and NMR spectroscopies, and HRMS.

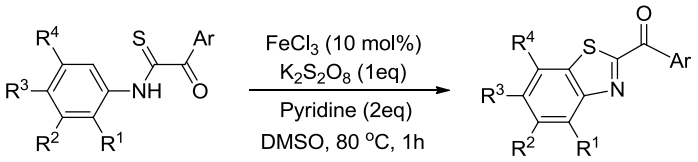
2-Benzoyl-6-methylbenzothiazole (2a)

White solid: mp 100–102 ℃ (Lit.[5n] 104–108 ℃). IR (KBr): 3059, 1640, 1597, 1570, 1493, 1292, 1118, 909, 852, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.50 (d, *J* = 7.6 Hz, 2H, ArH), 8.07 (d, *J* = 8.4 Hz, 1H, ArH), 7.75 (s, 1H, ArH), 7.62 (t, *J* = 7.2 Hz, 1H, ArH), 7.51 (t, *J* = 7.2 Hz, 2H, ArH), 7.35 (d, *J* = 8.4 Hz, 1H, ArH), 2.49 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 185.4, 166.1, 152.1, 138.3, 137.3, 135.1, 133.8, 131.2, 128.8, 128.5, 125.2, 121.7, 21.8. HRMS (ESI): *m/z* calcd for $C_{15}H_{11}NNaOS$ [$(M+Na)^+$], 276.0459; found, 276.0459.

2-Benzoyl-6-bromobenzothiazole (2b)

White solid; mp 121–123 ℃ (Lit.[8] 123–125 ℃); IR (KBr): 3099, 1642, 1594, 1535, 1478, 1287, 1123, 893, 703 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ = 8.56 (s, 1H, ArH), 8.42 (d, *J* = 6.6 Hz, 2H, ArH), 8.19 (d, *J* = 8.4 Hz, 1H, ArH), 7.80-7.75 (m, 2H, ArH), 7.65-7.59 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 184.9, 167.7, 152.7, 138.5, 134.7, 134.1, 131.3, 130.7, 128.6, 126.8, 124.8, 122.0.

Table 2. $FeCl_3$-catalyzed synthesis of 2-benzoylbenzothiazoles **2**



1 **2**

Entry	R^1	R^2	R^3	R^4	Ar	Product	Isolated Yield (%)
1	H	H	CH_3	H	C_6H_5	**2a**	86
2	H	H	Br	H	C_6H_5	**2b**	89
3	H	H	F	H	C_6H_5	**2c**	93
4	H	H	Cl	H	C_6H_5	**2d**	90
5	H	H	CH_3O	H	C_6H_5	**2e**	87
6	H	H	H	CH_3	C_6H_5	**2f**	83
7	Cl	H	H	H	C_6H_5	**2g**	83
8	H	H	F	Cl	4-$CH_3C_6H_4$	**2h**	90
9	H	H	H	CH_3	4-$CH_3C_6H_4$	**2i**	80
10	H	H	CH_3O	H	4-$CH_3C_6H_4$	**2j**	88
11	H	H	F	H	Furan-2-yl	**2k**	96
12	H	H	CH_3O	H	Furan-2-yl	**2l**	91
13	H	H	CH_3O	H	Thiophen-2-yl	**2m**	93
14	H	H	Cl	H	Thiophen-2-yl	**2n**	94
15	H	H	CH_3	H	2-ClC_6H_4	**2o**	87
16	H	H	CH_3O	H	4-BrC_6H_4	**2p**	85
17	H	H	Br	H	4-BrC_6H_4	**2q**	87
18	H	H	CH_3	H	4-$CH_3OC_6H_4$	**2r**	89
19	H	H	F	H	4-$CH_3OC_6H_4$	**2s**	89
20	H	H	Cl	H	4-ClC_6H_4	**2t**	85
21	H	H	EtO	H	4-$(CH_3)_3CC_6H_4$	**2u**	90

2-Benzoyl-6-fluorobenzothiazole (2c)

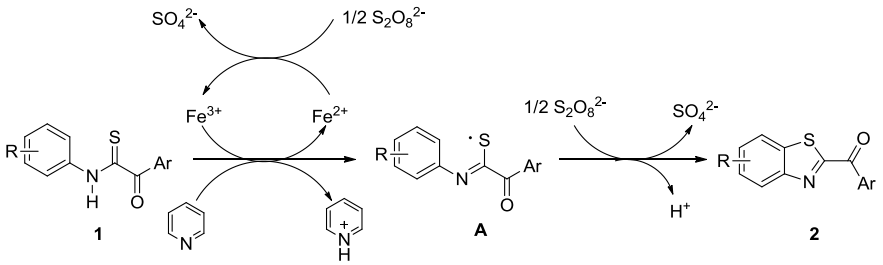
Light grey solid; mp 96–97 ℃ (Lit.[5n] 92–97 ℃); IR (KBr): 3086, 1641, 1598, 1563, 1497, 1440, 1248, 863, 704 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ = 8.42 (d, J = 6.9 Hz, 2H, ArH), 8.29–8.26 (m, 1H, ArH), 8.13 (d, J = 8.1 Hz, 1H, ArH), 7.76-7.73 (m, 1H, ArH), 7.64-7.60 (m, 2H, ArH), 7.54-7.50(m, 1H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6) δ = 185.0, 167.4, 161.8 (d, J_{CF} = 245.8 Hz), 150.6, 138.3, 138.1, 134.7 (d, J_{CF} = 9.5 Hz), 131.2, 129.1, 127.6 (d, J_{CF} = 9.9 Hz), 116.9 (d, J_{CF} = 25.4 Hz), 109.4 (d, J_{CF} = 25.9 Hz); HRMS (ESI): *m/z* calcd for $C_{14}H_8FNNaOS$ $[(M+Na)^+]$, 280.0208; found, 280.0200

6-Chloro-2-Benzoylbenzothiazole (2d)

White solid; mp 105–106 ℃ (Lit.[5n] 103–106 ℃). IR (KBr): 3126, 1657, 1588, 1533, 1483, 1292, 1095, 844, 712 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ = 8.44-8.40 (m, 3H, ArH), 8.26 (d, J = 8.4 Hz, 1H, ArH), 7.76 (d, J =6.3 Hz, 1H, ArH), 7.68-7.63 (m, 3H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6) δ = 185.1, 168.1, 152.4, 138.1, 134.7, 133.2, 131.3, 129.1, 128.5, 127.1, 122.9; HRMS (ESI): *m/z* calcd for $C_{14}H_8ClNNaOS$ $[(M+Na)^+]$, 295.9913; found, 295.9904.

2-Benzoyl-6-methoxybenzothiazole (2e)

White solid; mp 168–169 ℃ (Lit.[7] 171–173 ℃); IR (KBr): 3095,1640, 1607, 1494, 1452, 1258, 1229, 1017, 860, 708 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.54 (d, J = 7.2 Hz, 2H, ArH), 8.11 (d,



Scheme 2 Proposed mechanism of synthesis of 2-benzoylbenzothiazoles

J = 9.2 Hz, 1H, ArH), 7.66 (t, *J* = 7.6 Hz, 1H, ArH), 7.56 (t, *J* = 7.6 Hz, 2H, ArH), 7.43-7.42 (m, 1H, ArH), 7.26-7.18 (m, 1H, ArH), 3.93 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 185.2, 164.6, 159.8, 148.5, 139.1, 135.2, 133.7, 131.2, 128.5, 126.5, 117.7, 103.4, 55.9.

2-Benzoyl-7-methylbenzothiazole (2f)

Light yellow solid; mp 96–98 ℃; IR (KBr): 3121, 1642, 1597, 1480, 1440, 1291, 1123, 861, 784, 720 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ = 8.43 (d, *J* = 5.1 Hz, 2H, ArH), 8.10 (d, *J* = 7.2 Hz, 1H, ArH), 7.75 (d, *J* = 6.3 Hz, 1H, ArH), 7.65–7.55 (m, 3H, ArH), 7.47–7.44 (m, 1H, ArH), 2.59 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 185.4, 166.6, 153.8, 137.7, 135.0, 133.9, 132.2, 131.3, 128.5, 127.6, 127.2, 123.2, 21.4; HRMS (ESI): *m/z* calcd for $C_{15}H_{11}NNaOS$ $[(M+Na)^+]$, 276.0459; found, 276.0472.

4-Chloro-2-Benzoylbenzothiazole (2g)

White solid; mp 110–111 ℃ (Lit.[9] 110–112 ℃); IR (KBr): 3057, 1650, 1599, 1482, 1442, 1291, 1100, 888, 769 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ = 8.52-8.46 (m, 2H, ArH), 8.25-8.21 (m, 1H, ArH), 7.77-7.74 (m, 2H, ArH), 7.65-7.61 (m, 3H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 184.3, 167.8, 150.9, 138.4, 134.5, 134.2, 131.6, 130.5, 128.6, 128.1, 127.1, 120.7.

7-Chloro-6-fluoro-2-(4-methylbenzoyl)benzothiazole (2h)

Light grey solid; mp 150–152 ℃; IR (KBr): 3122, 1633, 1601, 1494, 1452, 1390, 1294, 1268, 1253,1184, 1093, 968, 891 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.46 (d, *J* = 8.0 Hz, 2H, ArH), 8.11–8.08 (m, 1H, ArH), 7.41 (d, *J* = 9.2 Hz, 1H, ArH), 7.38–7.34 (m, 2H, ArH), 2.47 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 183.7, 168.3, 157.3 (d, J_{CF} = 250.8 Hz), 150.1, 145.4, 139.1, 131.8, 131.7, 131.4, 129.3, 126.8, 125.0 (d, J_{CF} = 8.4 Hz), 116.6 (d, J_{CF} = 24.3 Hz), 113.8 (d, J_{CF} = 22.7 Hz), 109.0, 108.8, 21.9; HRMS (ESI): *m/z* calcd for $C_{15}H_9ClFNNaOS$ $[(M+Na)^+]$, 327.9975; found, 327.9974.

7-Methyl-2-(4-methylbenzoyl)benzothiazole (2i)

White solid; mp 112–114 ℃; IR (KBr): 3095, 1639, 1600, 1560, 1479, 1286, 1180, 1121, 864, 789 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.47 (d, *J* = 8.0 Hz, 2H, ArH), 8.08 (d, *J* = 8.4 Hz, 1H, ArH), 7.50 (t, *J* = 7.6 Hz, 1H, ArH), 7.32–7.37 (m, 3H, ArH), 2.65 (s, 3H, CH_3), 2.47 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 185.0, 166.9, 153.8, 144.9, 137.6, 132.5, 132.3, 131.4, 129.3, 127.4, 127.1, 123.1, 21.9, 21.4; HRMS (ESI): *m/z* calcd for $C_{16}H_{13}NNaOS$ $[(M+Na)^+]$, 290.0616; found, 290.0606.

2-(4-Methylbenzoyl)-6-methoxybenzothiazole (2j)

Light grey solid; mp 148–150 ℃; IR (KBr): 3094, 1634, 1604, 1492, 1450, 1255, 1229, 1180, 1020, 865, 830, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.45 (d, *J* = 7.6 Hz, 2H, ArH), 8.09 (d, *J* = 9.2 Hz, 1H, ArH), 7.40 (s, 1H, ArH), 7.34 (d, *J* = 7.6 Hz, 2H, ArH), 7.17 (d, *J* = 8.8 Hz, 1H, ArH), 3.91 (s, 3H, OCH_3), 2.46 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 184.7, 164.9, 159.6, 148.5, 144.7, 139.0, 132.6, 131.3, 129.2, 126.4, 117.5, 103.4, 55.8, 21.8; HRMS (ESI): *m/z* calcd for $C_{16}H_{13}NNaO_2$ $[(M+Na)^+]$, 306.0565; found, 306.0570.

(6-Fluorobenzo[*d*]thiazol-2-yl)(furan-2-yl)methanone (2k)

Grey solid; mp 144–146 ℃; IR (KBr): 3126, 1636, 1597, 1497, 1461, 1393, 1247, 1015, 840 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ = 8.33 (s, 1H, ArH), 8.17-8.14 (m, 1H, ArH), 7.83 (s, 1H, ArH), 7.66 (d, *J* = 7.6 Hz, 1H, ArH), 7.34-7.28 (m, 1H, ArH), 6.69 (s, 1H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6) δ = 173.5, 168.6, 163.8 (d, J_{CF} = 245.6 Hz), 153.2, 152.7, 151.4, 140.1 (d, J_{CF} = 11.8 Hz), 129.6 (d, J_{CF} = 9.4 Hz), 128.0, 119.2 (d, J_{CF} = 25.3 Hz), 116.1, 111.7 (d, J_{CF} = 27.2 Hz); HRMS (ESI): *m/z* calcd for $C_{12}H_6FNNaO_2S$ $[(M+Na)^+]$, 270.0001; found, 270.0012.

(Furan-2-yl)(6-methoxybenzo[*d*]thiazol-2-yl)methanone (2l)

Light yellow solid; mp 208–210 ℃; IR (KBr): 3086, 1629, 1603, 1495, 1465, 1399, 1259, 1230, 1024, 839, 797, 755 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ = 8.29-8.24 (m, 2H, ArH), 8.15 (d, *J* = 8.4 Hz, 1H, ArH), 7.81 (s, 1H, ArH), 7.27 (d, *J* = 8.4 Hz, 1H, ArH), 6.88 (s, 1H, ArH), 3.89 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 172.1, 163.4, 159.7, 149.9, 148.6, 148.4, 138.9, 126.2, 124.5, 117.7, 112.8, 103.4, 55.9; HRMS (ESI): *m/z* calcd for $C_{13}H_9NNaO_3S$ $[(M+Na)^+]$, 282.0201; found, 282.0200.

(6-Methoxybenzo[*d*]thiazol-2-yl)(thiophen-2-yl)methanone (2m)

Light yellow solid; mp 162–164 ℃. IR (KBr): 3065, 1621, 1605, 1495, 1410, 1256, 1230, 1038, 833 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.71 (s, 1H, ArH), 8.09 (s, 1H, ArH), 7.80 (s, 1H, ArH), 7.38 (s, 1H, ArH), 7.18 (s, 2H, ArH), 3.91 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 176.9, 164.0, 159.7, 148.3, 139.8, 139.1, 137.0, 136.4, 128.4, 126.3, 117.7, 103.5, 55.9; HRMS (ESI): *m/z* calcd for $C_{13}H_9NNaO_2S_2$ $[(M+Na)^+]$, 297.9972; found, 297.9986.

(6-Chlorobenzo[*d*]thiazol-2-yl)(thiophen-2-yl)methanone (2n)

Light grey solid; mp 140–142 ℃; IR (KBr): 3088, 1630, 1485,1410, 1294, 1124, 1087, 1038, 813, 785, 718 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.74 (s, 1H, ArH), 8.13 (d, *J* = 8.4 Hz, 1H, ArH), 7.97 (s, 1H, ArH), 7.85-7.84 (m, 1H, ArH), 7.54 (d, *J* = 8.8 Hz, 1H, ArH), 7.26 (s, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 176.6, 167.1, 152.2, 139.5, 138.1, 137.5, 137.0, 133.9, 128.5, 128.0, 126.3, 121.8; HRMS (ESI): *m/z* calcd for $C_{12}H_6ClNNaOS_2$ $[(M+Na)^+]$, 301.9477; found, 301.9455.

2-(2-Chlorobenzoyl)-6-methylbenzothiazole (2o)

Light yellow solid; mp 164–166 ℃; IR (KBr): 3079, 1658, 1588, 1485, 1433, 1297, 1267, 909, 857, 813, 744 cm^{-1}; ^1H NMR (400

MHz, $CDCl_3$) δ = 8.03 (d, J = 8.4 Hz, 1H, ArH), 7.79 (s, 1H, ArH), 7.77–7.73 (m, 1H, ArH), 7.53–7.46 (m, 2H, ArH), 7.43–7.39 (m, 1H, ArH), 7.3–7.36 (m, 1H, ArH), 2.52 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 187.7, 164.9, 152.0, 138.8, 137.8, 136.1, 132.6, 132.3, 130.8, 130.5, 129.0, 126.5, 125.5, 121.9, 21.9; HRMS (ESI): *m/z* calcd for $C_{15}H_{10}ClNNaOS$ [(M+Na)$^+$], 310.0069; found, 310.0057.

2-(4-Bromobenzoyl)-6-methoxybenzothiazole (2p)

Light yellow solid; mp 192–195 ℃ (Lit.[5o] 197–199 ℃) ℃; IR (KBr): 3090, 1637, 1604, 1496, 1448, 1257, 1114, 1016, 910, 863, 832, 747 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.44 (s, 2H, ArH), 8.08 (s, 1H, ArH), 7.69 (s, 2H, ArH), 7.40 (s, 1H, ArH), 7.19 (s, 1H, ArH), 3.93 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 184.0, 164.2, 159.9, 148.5, 139.2, 133.9, 132.7, 131.8, 129.2, 126.5, 117.8, 103.4, 55.9; HRMS (ESI): *m/z* calcd for $C_{15}H_{10}BrNNaO_2S$ [(M+Na)$^+$], 369.9513; found, 369.9493.

2-(4-Bromobenzoyl)-6-bromobenzothiazole (2q)

Light yellow solid; mp 160–161 ℃; IR (KBr): 3092, 1642, 1584, 1477, 1397, 1289, 1124, 1075, 891, 836, 751 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.44 (d, J = 7.6 Hz, 2H, ArH), 8.16 (s, 1H, ArH), 8.08 (d, J = 8.8 Hz, 1H, ArH), 7.70 (d, J = 6.8 Hz, 3H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 182.7, 166.2, 151.5, 137.5, 132.3, 131.7, 130.9, 129.8, 128.7, 125.7, 123.7, 121.2; HRMS (ESI): *m/z* calcd for $C_{14}H_7Br_2NNaOS$ [(M+Na)$^+$], 417.8513; found, 417.8509.

2-(4-Methoxybenzoyl)-6-methylbenzothiazole (2r)

Light yellow solid; mp 138–139 ℃ (Lit.[9] 137–139 ℃); IR (KBr): 3033, 2913, 1632, 1603, 1494, 1301, 1267, 1118, 1031, 911, 860, 814, 760 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.63 (d, J = 8.4 Hz, 2H, ArH), 8.09 (d, J = 8.4 Hz, 1H, ArH), 7.77 (s, 1H, ArH), 7.37 (d, J = 8.4 Hz, 1H, ArH), 7.03 (d, J = 8.4 Hz, 1H, ArH), 3.91 (s, 3H, OCH_3), 2.52 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 183.7, 167.2, 164.6, 152.4, 138.4, 137.5, 134.1, 129.0, 128.2, 125.4, 122.0, 114.2, 55.9, 22.2; HRMS (ESI): *m/z* calcd for $C_{16}H_{13}NNaO_2S$ [(M+Na)$^+$], 306.0565; found, 306.0575.

6-Fluoro-2-(4-Methoxybenzoyl)benzothiazole (2s)

Light yellow solid; mp 146–148 ℃; IR (KBr): 3097, 1632, 1603, 1564, 1501, 1448, 1304, 1250, 1177, 1111, 869, 840, 760 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.56 (d, J = 8.4 Hz, 2H, ArH), 8.18–8.17 (m, 1H, ArH), 7.66 (d, J = 8.0 Hz, 1H, ArH), 7.33–7.29 (m, 1H, ArH), 7.14 (d, J = 8.4 Hz, 1H, ArH), 3.91 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 181.8, 166.8, 163.4, 160.8 (d, J_{CF} = 248.2 Hz), 149.5, 137.1 (d, J_{CF} = 11.2 Hz), 132.8, 126.5, 125.8 (d, J_{CF} = 9.6 Hz), 115.0 (d, J_{CF} = 25.1 Hz), 112.9, 107.1 (d, J_{CF} = 26.5 Hz), 54.6; HRMS (ESI): *m/z* calcd for $C_{15}H_{11}FNO_2S$ [(M+Na)$^+$], 288.0495; found, 288.0471.

6-Chloro-2-(4-chlorobenzoyl)benzothiazole (2t)

Light yellow solid; mp 136–138 ℃; IR (KBr): 3089, 1638, 1586, 1479, 1294, 1134, 1095, 898, 842, 810, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.54 (d, J = 8.8 Hz, 2H, ArH), 8.14 d, J = 8.8 Hz, 1H, ArH), 7.99 (s, 1H, ArH), 7.56–7.52 (m, 3H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 184.5, 167.3, 152.3, 140.8, 138.1, 134.2, 132.9, 132.7, 128.9, 128.1, 126.5, 121.8; HRMS (ESI): *m/z* calcd for $C_{14}H_7Cl_2NNaOS$ [(M+Na)$^+$], 329.9523; found, 329.9499.

2-(4-*tert*-butylbenzoyl)-6-ethoxybenzothiazole (2u)

Light yellow solid; mp 108–110 ℃; IR (KBr): 3080, 2970, 1633, 1601, 1492, 1250, 1223, 1191, 1054, 899, 861, 726 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.48 (d, J = 8.8 Hz, 2H, ArH), 8.07 (d, J = 9.2 Hz, 1H, ArH), 7.56 (d, J = 8.8 Hz, 2H, ArH), 7.37 (s, 1H, ArH), 7.16-7.14 (m, 1H, ArH), 4.14-4.09 (m, 2H, CH_2), 1.47 (t, J = 6.8 Hz, 3H, CH_3), 1.37 (s, 9H, 3×CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 183.7, 163.8, 158.0, 156.4, 147.4, 138.0, 131.5, 130.1, 125.3, 124.5, 116.8, 102.9, 63.1, 34.2, 30.1, 13.7; HRMS (ESI): *m/z* calcd for $C_{20}H_{21}NNaO_2S$ [(M+Na)$^+$], 362.1191; found, 362.1202.

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