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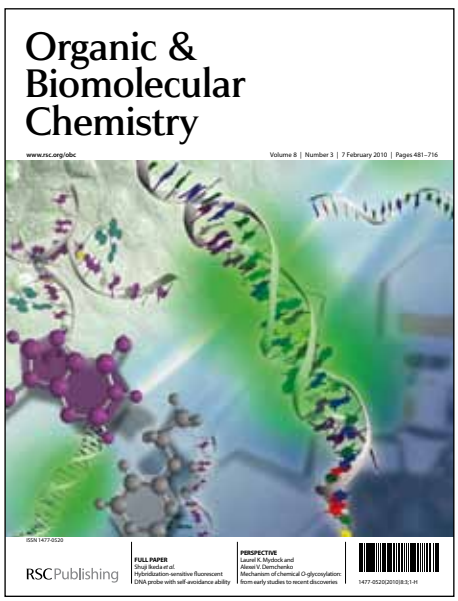

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ARTICLE TYPE

Cu-Catalyzed Direct C-H Bond Functionalization: A Regioselective Protocol to 5-Aryl Thiazolo[3,2-*b*]-1,2,4-triazoles

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An efficient, regioselective C-5 arylation of thiazolo[3,2-*b*]-1,2,4-triazoles catalyzed by the simple copper catalyst was developed. This arylation proceeded smoothly and tolerated a variety of functional groups (44 examples). A wide range of functionalized thiazolo[3,2-*b*]-1,2,4-triazole derivatives were obtained in high yields (up to 99% yield). Possible catalytic cycles of the arylation was also discussed.

Introduction

Heteroaromatic compounds are widespread in various natural products[1] of enormous practical importance, ranging from pharmaceutical agents and biological probes to electroactive materials.[2] As a number of representatives of this class, thiazolo[3,2-*b*]-1,2,4-triazole derivatives are highly attractive heterocyclic units because of their diverse biological activity.[3-10] Examples of well-known thiazolo[3,2-*b*]-1,2,4-triazole derivatives include anthelmintics,[3] antimicrobial,[4] medicinal fungicides,[5] cardiotonics, bronchodilators,[6] analgesic, anti-inflammatory,[7] antipyretic,[7b] anticancer[8] and vasodilatory drugs.[9] As a classical example, in 1990s, Shibahara *et al*[10] described the identification and characterization of several molecules bearing thiazolo[3,2-*b*]-1,2,4-triazoles as an activator of cephalosporins, which had a minimum inhibitory concentration of 0.39 μg/mL against *staphylococcus aureus* and could be used as a therapeutic medicine for microbisms.

In general, the thiazolo[3,2-*b*]-1,2,4-triazole derivatives were usually obtained by fusion of the heteroaromatic cycles with the desired substituent at oriented position.[8,11] To the best of our knowledge, example of direct and regioselective arylation of the thiazolo[3,2-*b*]-1,2,4-triazole core has not been reported thus far.

In recent years, transition-metal-catalyzed direct C-H functionalization has received a great deal of attention,[12] and a wide range of metal catalysts have undergone explosive growth in the past few years.[13] Compared with those catalysts, inexpensive copper, as the first transition metal, has been used to promote C-H bond functionalization by Hofmann[14] and Zechmeister[15] who had made a significant breakthrough. Although there has been remarkable progress in copper-catalyzed C-H bond functionalization since then,[16] the applicable catalysts still remain limited. Therefore, there is still an interesting topic to develop and construct new heteroaromatic compounds by copper-catalyzed direct C-H functionalization with simpler catalytic systems and much milder conditions.

Inspired by the successful results in our recent research about the arylation of imidazo[2,1-*b*]thiazoles,[17a] we attempt the direct arylation of thiazolo[3,2-*b*]-1,2,4-triazole to develop new derivatives. Although from the standpoint of the "scaffold" between thiazolo[3,2-*b*]-1,2,4-triazoles and imidazo[2,1-*b*]thiazoles, only one atom is different, they showed a big difference in biological activity.[17b] Herein, we develop a novel synthetic route for 5-arylated thiazolo[3,2-*b*]-1,2,4-triazoles catalyzed by copper catalyst, compatible with a variety of functional groups. It is also the first example that the direct arylation of thiazolo[3,2-*b*]-1,2,4-triazoles are accomplished so far.

Results and discussion

Initially, 6-phenylthiazolo[3,2-*b*]-1,2,4-triazole (**1a**), which was synthesized according to the literature method,[18] was selected to test the arylation. The arylation reaction was performed with **1a** and iodobenzene **2a** as reactants, *t*-BuOLi as a base, and DMF-Xylene as mixture solvent. As shown in Table 1, eleven types of simple copper salts were tested at 120 °C for 12 h (entries 1-11). To our surprise, the results showed not only high yields, but also only C-5 arylated products. Among those eleven copper salts, $Cu(acac)_2$ afforded the highest yield (entries 10), instead of CuCl, which was the best copper salt we previously reported for the arylation of imidazo[2,1-*b*]thiazoles.[17a] Subsequently, with the catalyst $Cu(acac)_2$, we investigated the solvent effect for this arylation reaction. As shown in Table 1 (entry 10, 12-17), two good results were obtained in DMF and DMF-Xylene mixtures

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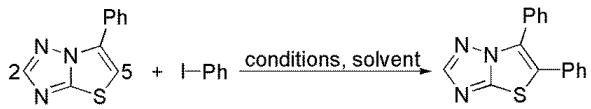
† Electronic Supplementary Information (ESI) available: General experimental procedures, spectral data and copies of ^{1}H NMR and ^{13}C NMR spectra. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b000000x/

(entries 10 and 12), and the latter provided higher yield. And then we explored the effects of the temperature, Cu-catalyst loading and base, respectively, in this arylation reaction.[19] The reaction yield decreased when the reaction temperature was reduced to 100 °C or room temperature from 120 °C, and the yield did not increase when the temperature was raised to 140 °C. Decreasing the amount of addtion of $Cu(acac)_2$ negatively affects the yield of the arylated product, as does lowering the reaction temperature. Reducing the $Cu(acac)_2$ catalyst loading from 20 to 10 and then 5 mol % lowered the yields of product from 98% to 87% and 66%, respectively. In the absence of the Cu catalyst, no arylated product was found, and on the other hand, the yield could not increase when the $Cu(acac)_2$ loading was raised to 40 mol %. With these above optimized arylation conditions, the effects of bases were investigated. It was found that a variety of weak inorganic bases (K_2CO_3, Cs_2CO_3 and K_3PO_4) were unsuitable for the arylation ascribed to the poor yields. Compared to *t*-BuOLi, we also tested other alkoxide bases, *t*-BuOK and *t*-BuONa, and lower yields of 56% and 47% were obtained. Specially noted, no arylated product was found without bases. The above experiments demonstrated that the optimized conditions for the C-5 arylation of thiazolo[3,2-*b*]-1,2,4-triazoles are: $Cu(acac)_2$ (20 mol %) and *t*-BuOLi (2.0 equiv) in DMF-Xylene at 120 °C. Moreover, PhBr and PhCl, as substitutes instead of PhI also were tested, and only PhBr gave traces of C-5 arylated product under the above optimized conditions.

Table 1. Cu-catalyzed Arylation of Thiazolo[3,2-*b*]-1,2,4-triazole[a]



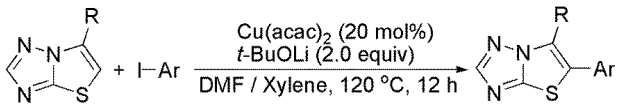
1a **2a** **3aa**

Entry	Conditions	Solvent	Yield(%)[b]
1	CuCl	DMF/Xylene (1:1)	66
2	CuBr	DMF/Xylene (1:1)	85
3	CuI	DMF/Xylene (1:1)	74
4	CuCN	DMF/Xylene (1:1)	70
5	$CuCl_2$	DMF/Xylene (1:1)	82
6	$CuBr_2$	DMF/Xylene (1:1)	62
7	$CuCl_2·2H_2O$	DMF/Xylene (1:1)	75
8	$CuSO_4·5H_2O$	DMF/Xylene (1:1)	71
9	$Cu(OAc)_2·H_2O$	DMF/Xylene (1:1)	79
10	$Cu(acac)_2$	DMF/Xylene (1:1)	98
11	$Cu(OTf)_2$	DMF/Xylene (1:1)	68
12	$Cu(acac)_2$	DMF	93
13	$Cu(acac)_2$	Xylene	42
14	$Cu(acac)_2$	NMP	51
15	$Cu(acac)_2$	Toluene	82
16	$Cu(acac)_2$	1,4-Dioxene	43
17	$Cu(acac)_2$	DMA	38

[a] The reaction was performed with **1a** (0.5 mmol), **2a** (1.0 mmol) and *t*-BuOLi (2.0 equiv) in 1mL of solvent at 120 °C for 12 h. [b] Isolated yield

The scope on the copper-catalyzed C-H arylation of thiazolo[3,2-*b*]-1,2,4-triazoles **1** and aryl iodides **2** was investigated under the above optimized conditions (Table 2). As shown in Table 2, it was found that the electron-deficient and electron-rich aryl iodides were reactive and the corresponding target products were obtained in good to excellent yields (entries 1-11). It was noteworthy that electron-rich aryl iodides gave a little higher yield than electron-deficient ones (entries 2, 5, 6, 7, 8 vs entries 3, 4, 9, 10). Most interestingly, this arylation was not sensitive to the sterically hindered factors of aryl iodides and gave excellent yield (entries 11, 22, 33, 44). Furthermore, other different substituted thiazolo[3,2-*b*]-1,2,4-triazoles, such as 6-(4-bromophenyl)thiazolo[3,2-*b*]-1,2,4-triazole, 6-*p*-tolylthiazolo[3,2-*b*]-1,2,4-triazoe, 6-methylthiazolo[3,2-*b*]-1,2,4-triazole were also tested and afforded the corresponding products in excellent yields. It should be noted that the substrates **1** with electron-rich aromatic groups gave slightly better yields than the electron-deficient aromatic groups (entries 12-22 vs 23-33). We also found the substrates **1** with aromatic groups gave better yields than the

Table 2. Scope of Cu-catalyzed Arylation of Thiazolo[3,2-*b*]-1,2,4-triazoles[a]



1 **2** **3**

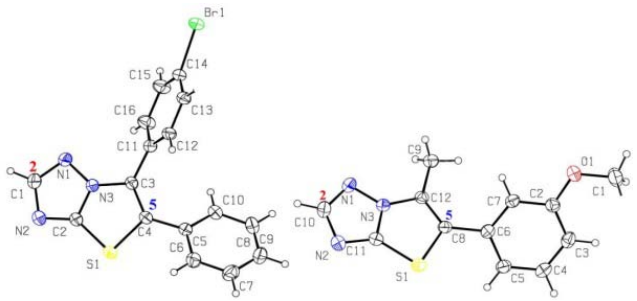
Entry	R	Ar	Products	Yield (%)[b]
1	C_6H_5	C_6H_5	**3aa**	98
2	C_6H_5	3-$CH_3OC_6H_4$	**3ab**	94
3	C_6H_5	4-FC_6H_4	**3ac**	89
4	C_6H_5	4-$CF_3C_6H_4$	**3ad**	85
5	C_6H_5	4-$CH_3C_6H_4$	**3ae**	91
6	C_6H_5	4-$CH_3OC_6H_4$	**3af**	93
7	C_6H_5	4-$C(CH_3)_3C_6H_4$	**3ag**	90
8	C_6H_5	2-$C_2H_5C_6H_4$	**3ah**	96
9	C_6H_5	2-ClC_6H_4	**3ai**	88
10	C_6H_5	3-FC_6H_4	**3aj**	82
11	C_6H_5	1-naphthyl	**3ak**	97
12	4-BrC_6H_4	C_6H_5	**3ba**	95
13	4-BrC_6H_4	3-$CH_3OC_6H_4$	**3bb**	92
14	4-BrC_6H_4	4-FC_6H_4	**3bc**	86
15	4-BrC_6H_4	4-$CF_3C_6H_4$	**3bd**	79
16	4-BrC_6H_4	4-$CH_3C_6H_4$	**3be**	90
17	4-BrC_6H_4	4-$CH_3OC_6H_4$	**3bf**	91
18	4-BrC_6H_4	4-$C(CH_3)_3C_6H_4$	**3bg**	94
19	4-BrC_6H_4	2-$C_2H_5C_6H_4$	**3bh**	93
20	4-BrC_6H_4	2-ClC_6H_4	**3bi**	85
21	4-BrC_6H_4	3-FC_6H_4	**3bj**	80
22	4-BrC_6H_4	1-naphthyl	**3bk**	95
23	4-$CH_3C_6H_4$	C_6H_5	**3ca**	98
24	4-$CH_3C_6H_4$	3-$CH_3OC_6H_4$	**3cb**	96
25	4-$CH_3C_6H_4$	4-FC_6H_4	**3cc**	91
26	4-$CH_3C_6H_4$	4-$CF_3C_6H_4$	**3cd**	88
27	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	**3ce**	92
28	4-$CH_3C_6H_4$	4-$CH_3OC_6H_4$	**3cf**	93
29	4-$CH_3C_6H_4$	4-$C(CH_3)_3C_6H_4$	**3cg**	92
30	4-$CH_3C_6H_4$	2-$C_2H_5C_6H_4$	**3ch**	95
31	4-$CH_3C_6H_4$	2-ClC_6H_4	**3ci**	88
32	4-$CH_3C_6H_4$	3-FC_6H_4	**3cj**	83
33	4-$CH_3C_6H_4$	1-naphthyl	**3ck**	96
34	CH_3	C_6H_5	**3da**	90
35	CH_3	3-$CH_3OC_6H_4$	**3db**	98
36	CH_3	4-FC_6H_4	**3dc**	83
37	CH_3	4-$CF_3C_6H_4$	**3dd**	76
38	CH_3	4-$CH_3C_6H_4$	**3de**	93
39	CH_3	4-$CH_3OC_6H_4$	**3df**	92
40	CH_3	4-$C(CH_3)_3C_6H_4$	**3dg**	99
41	CH_3	2-$C_2H_5C_6H_4$	**3dh**	94
42	CH_3	2-ClC_6H_4	**3di**	87
43	CH_3	3-FC_6H_4	**3dj**	81
44	CH_3	1-naphthyl	**3dk**	93

[a]The reaction was performed with **1** (0.5 mmol), **2** (1.0 mmol), *t*-BuOLi (2.0 equiv), and $Cu(acac)_2$ (20 mol %) in 1 mL of DMF/Xylene at 120 °C for 12 h. [b] Isolated yield after column chromatography of the crude.

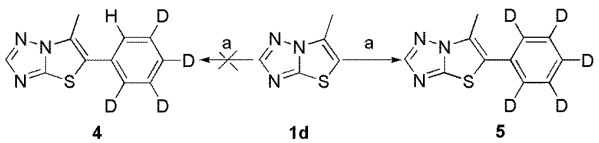
aliphatic groups (entries 1 vs 34).

Single crystals of **3ba** and **3db** were obtained successfully, and their structures were unambiguously confirmed further by X-ray crystallography analysis (Figure 1).[19] As shown clearly in Figure 1, C-5 arylation rather than C-2 arylation occurred, although C-2 arylation remained dominant from the standpoint of the steric effect.

Figure 1. Crystal structure of product **3ba** (left) and **3db** (right)

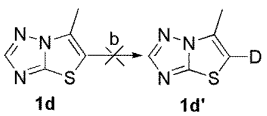


Naturally, we attempted to understand the mechanism for this arylation reaction. Firstly, 6- methylthiazolo[3,2-*b*]-1,2,4-triazole and C_6D_5I were used as starting materials under the optimized conditions for mechanistic studies (Scheme 1a). Only compound **5** were obtained in the above reaction, and **4** was not found. It meant no H-D exchange occurred, and this observation eliminated the assumption that the reaction proceeded via a copper-assisted benzyne-type mechanism.[20] Secondly; the results also could eliminate the assumption that the reaction proceeded *via* Friedel-Crafts alkylations for the reason that no arylated product was found without bases. Thirdly, *t*-BuOLi as a base was not strong enough to remove the H-5 directively according to our experimental result (Scheme 1b), so the deprotonation-metalation mechanism[16b] could also be eliminated in this arylation reaction.



4 **1d** **5**

(a): C_6D_5I, $Cu(acac)_2$, *t*-BuOLi, DMF/xylene

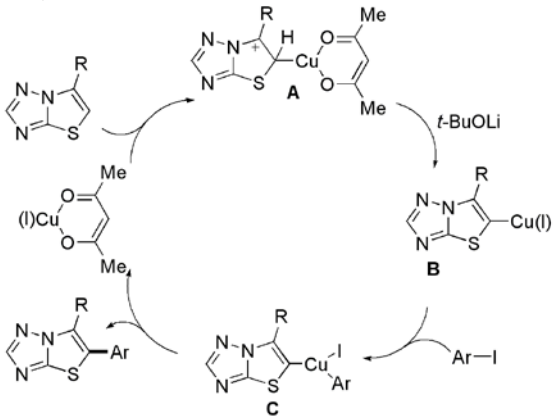


1d **1d'**

(b): (i) *t*-BuOLi/DMF/Xylene; (ii) D_2O

Scheme 1. Mechanistic Studies

Consequently, the possible catalytic cycles was suggested in Scheme 2. Initially, $Cu(acac)_2$ would be reduced to the active monovalent specie,[21] and then the addition between Cu(I) and heterocycle gave the cationic intermediates **A**, following the deprotonation by the base to give the organocopper specie **B**,[22] which possibly underwent the oxidative addition to give the Cu(III)-aryl specie **C**. Finally, the desired arylation product was obtained by a reductive elimination from **C** releasing the Cu(I) catalyst.[16f] The thiazolo[3,2-*b*]-1,2,4-triazole substrate was composed of π-deficient triazole ring and π-excessive thiazole ring. Cu(III)-aryl specie **C** formed at C-5 of the π-excessive thiazole ring was proposed to be a key intermediate of the catalytic cycle. Moreover, Cu(III)-aryl specie **C** formed with electron-rich aryl iodides was more stable than electron-deficient one, which was why the former gave higher yields than the latter one (Table 2). Futhermore, this mechanism can also explain the aromatic substrates gave better results than the aliphatic one (Table 2).



Scheme 2. Possible Catalytic Cycle for Cu-catalyzed Regioselective Arylation of Thiazolo[3,2-*b*]-1,2,4-triazoles

Conclusions

In conclusion, we have developed a new copper-catalyzed methodology for the direct, efficient and regioselective C-5 arylation of thiazolo[3,2-*b*]-1,2,4-triazoles. A variety of substituents on both thiazolo[3,2-*b*]-1,2,4-triazoles and aryl iodides were tolerated. In this arylation, the simple $Cu(acac)_2$ was utilized as the catalyst, and the arylated thiazolo[3,2-*b*]-1,2,4-triazole derivitives were obtained in high to excellent yields. This method provides not only a new and useful strategy for the construction of biologically active heteroaromatic molecules, but also a new approach for developing Cu-catalyzed C-H functionalization. Further research will focus on the more detailed machnism, and the application of copper in the synthesis of other biological heteroaromatic compounds.

Experimental

General information

^1H and ^{13}C NMR spectra were recorded on a Bruker DPX 300 MHz spectrometer in $CDCl_3$ or d_6-DMSO solution. ESI-MS spectra were measured on Finnigan Mat TSQ 7000 instruments. High-resolution electrospray ionization mass spectra (HR-ESI-MS) were recorded on an Agilent 6540Q-TOF LCMS equipped with an electrospray ionization (ESI) probe operating in positive-ion mode with direct infusion. Melting points (mp) were determined with a digital electrothermal apparatus without further correction. Analytical HPLC was performed on a Shimadzu™ LC-10A system via a VP-ODS C18 column (250 mm × 4.6 mm, 5 μm particle size) with a CH_3CN-H_2O mobile phase. TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel $60F_{254}$. Silica gel (200-300 mesh) was used for column chromatography. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Solvents were freshly distilled prior

to use. Chemical shifts for ^{1}H NMR are expressed in parts per million (ppm) relative to tetramethylsilane (δ 0.0 ppm). Chemical shifts for ^{13}C NMR are expressed in ppm relative to $CDCl_3$ (δ 77.16 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, bs = broad singlet), coupling constant (Hz), and integration. All reactions were carried out under nitrogen atmosphere unless noted.

Typical Procedure for the Cu-catalyzed Regioselective Arylation of Thiazolo[3,2-*b*]-1,2,4-triazoles with Aryl Iodides

A suspension of thiazolo[3,2-*b*]-1,2,4-triazoles (0.50 mmol), $Cu(acac)_2$ (26.0 mg, 0.10 mmol, 20 mol %), *t*-BuOLi (80.0 mg, 1.00 mmol, 2.0 equiv), and aryl iodides (1.00 mmol) in DMF/Xylene (0.5/0.5 mL) was stirred at room temperature for 5 min under N_2 and heated in oil bath (120 ^{o}C) for 12 h. The reaction mixture was allowed to cool to room temperature and diluted with ethyl acetate (25 mL). The resulting solution was washed with brine (3×10 mL), dried over anhydrous Na_2SO_4 and concentrated under vacuum to a volume of about 2 mL. The mixture containing the product was subjected to flash chromatography on silica gel (ethyl acetate / petroleum ether mixtures) to afford target arylation product.

5,6-Diphenylthiazolo[3,2-*b*]-1,2,4-triazole (3aa, Known Compound)

Colorless solid. Yield: 98% (136 mg). Mp: 191-193 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.26 (s, 1H), 7.63-7.60 (m, 2H), 7.44-7.42 (m, 3H), 7.36 (s, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.8, 131.2, 129.8, 129.3, 129.1, 128.9, 128.6, 127.9, 127.2. ESI-MS m/z (%) 278.09 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{16}H_{11}N_3S$ $[MH^+]$: 278.0746; Found: 278.0749.

5-(3-Methoxyphenyl)-6-phenylthiazolo[3,2-*b*]-1,2,4-triazole (3ab)

Colorless oil. Yield: 94% (144 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.65-7.62 (m, 2H), 7.45-7.43 (m, 3H), 7.26 (d, J = 15.8 Hz, 1H), 6.96-6.87 (m, 3H), 3.69 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.8, 155.2, 132.3 130.1, 129.8, 128.8, 128.3, 127.8, 127.1, 126.6, 121.5, 114.9, 55.2. ESI-MS m/z (%) 308.05 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{17}H_{13}N_3OS$ $[MH^+]$: 308.0852; Found: 308.0856.

5-(4-Fluorophenyl)-6-phenylthiazolo[3,2-*b*]-1,2,4-triazole (3ac)

Colorless solid. Yield: 89% (131 mg). Mp: 186-188 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.25 (s, 1H), 7.61-7.58 (m, 2H), 7.45-7.43 (m, 3H), 7.37-7.32 (m, 2H), 7.06 (t, J = 8.5 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.0 (J_{CF} = 250.6 Hz), 155.9, 131.3 (J_{CF} = 8.2 Hz), 129.9, 129.7, 128.9, 128.7, 127.7, 127.3, 127.2, 125.9, 116.3 (J_{CF} = 22.0 Hz). ESI-MS m/z (%) 296.05 (100) $[M+H]^+$. HRMS (ESI) calcd. For $C_{16}H_{10}FN_3S$ $[MH^+]$: 296.0652; Found: 296.0655.

5-(4-(Trifluoromethyl)phenyl)-6-phenylthiazolo[3,2-*b*]-1,2,4-triazole (3ad)

Colorless solid. Yield: 85% (147 mg). Mp: 141-143 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.21 (s, 1H), 7.63-7.59 (m, 4H), 7.50-7.46 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.6, 134.9, 130.2, 129.8, 129.6, 129.1, 127.2, 126.1, 126.0, 125.4. ESI-MS m/z (%) 345.95 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{17}H_{10}F_3N_3S$ $[MH^+]$: 346.0620; Found: 346.0624.

6-Phenyl-5-*p*-tolylthiazolo[3,2-*b*]-1,2,4-triazole (3ae)

Colorless solid. Yield: 91% (133 mg). Mp: 182-184 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.64-7.61 (m, 2H), 7.44-7.42 (m, 3H), 7.25 (d, J = 8.1 Hz, 2H), 7.15 (d, J = 8.1 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.1, 139.3, 129.8, 129.7, 129.6, 129.2, 128.8, 128.2, 127.9, 127.5, 21.3. ESI-MS m/z (%) 291.95 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{17}H_{13}N_3S$ $[MH^+]$: 292.0903; Found: 292.0907.

5-(4-Methoxyphenyl)-6-phenylthiazolo[3,2-*b*]-1,2,4-triazole (3af)

Colorless solid. Yield: 93% (143 mg). Mp: 113-115 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.64-7.61 (m, 2H), 7.44-7.42 (m, 3H), 7.29 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 3.83 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.2, 155.0, 130.7, 129.7, 129.6, 128.8, 127.9, 127.6, 127.3, 123.3, 54.9. ESI-MS m/z (%) 307.95 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{17}H_{13}N_3OS$ $[MH^+]$: 308.0852; Found: 308.0856.

5-(4-*t*-butylphenyl)-6-phenylthiazolo[3,2-*b*]-1,2,4-triazole (3ag)

Colorless solid. Yield: 90% (150 mg). Mp: 125-127 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.66-7.62 (m, 2H), 7.46-7.44 (m, 3H), 7.36 (d, J = 8.6 Hz, 2H), 7.29 (d, J = 8.6 Hz, 2H), 1.32 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.1, 154.4, 152.4, 129.8, 129.7, 128.8, 128.2, 127.9, 127.8, 127.5, 126.0, 34.8, 31.2. ESI-MS m/z (%) 334.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{20}H_{19}N_3S$ $[MH^+]$: 334.1372; Found: 334.1377.

5-(2-Ethylphenyl)-6-phenylthiazolo[3,2-*b*]-1,2,4-triazole (3ah)

Colorless solid. Yield: 96% (147 mg). Mp: 108-110 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.23 (s, 1H), 7.60-7.56 (m, 2H), 7.43-7.24 (m, 7H), 2.49 (q, J = 7.5 Hz, 2H), 1.01 (t, J = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.1, 143.9, 139.4, 132.0, 129.4, 129.2, 128.7, 128.6, 128.4, 127.9, 127.5, 126.3, 125.9, 26.0, 14.8. ESI-MS m/z (%) 306.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{18}H_{15}N_3S$ $[MH^+]$: 306.1059; Found: 306.1062.

5-(2-Chlorophenyl)-6-phenylthiazolo[3,2-*b*]-1,2,4-triazole (3ai)

Colorless solid. Yield: 88% (137 mg). Mp: 147-149 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.22 (s, 1H), 7.60-7.56 (m, 2H), 7.50-7.27 (m, 7H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.3, 135.1, 133.3, 131.1, 130.4, 129.7, 128.8, 128.7, 127.6, 127.3, 123.4. ESI-MS m/z (%) 311.95 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{16}H_{10}ClN_3S$ $[MH^+]$: 312.0357; Found: 312.0359.

5-(3-Fluorophenyl)-6-phenylthiazolo[3,2-*b*]-1,2,4-triazole (3aj)

Colorless solid. Yield: 82% (121 mg). Mp: 151-153 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.19 (s, 1H), 7.63-7.60 (m, 2H), 7.47-7.45 (m, 3H), 7.34 (dd, J = 14.5, 7.1 Hz, 1H), 7.17-7.05 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.8 (J_{CF} = 248.2 Hz), 155.4, 154.5, 133.3, 133.2, 130.8 (J_{CF} = 8.5 Hz), 130.1, 129.7, 129.0, 127.3, 125.6, 125.1 (J_{CF} = 2.6 Hz), 116.2 (J_{CF} = 22.1 Hz). ESI-MS m/z (%) 295.95 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{16}H_{10}FN_3S$ $[MH^+]$: 296.0652; Found: 296.0658.

5-(Naphthalen-1-yl)-6-phenylthiazolo[3,2-*b*]-1,2,4-triazole (3ak)

Yellow solid. Yield: 97% (159 mg). Mp: 142-144 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.27 (s, 1H), 7.96-7.89 (m, 3H), 7.60-7.43 (m, 6H), 7.30-7.21 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.5, 155.0, 133.7, 132.0, 130.5, 130.3, 129.4, 128.7, 128.5, 127.3, 126.6, 125.4, 125.1. ESI-MS m/z (%) 328.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{20}H_{13}N_3S$ $[MH^+]$: 328.0903; Found: 328.0906.

6-(4-Bromophenyl)-5-phenylthiazolo[3,2-*b*]-1,2,4-triazole (3ba)

Colorless solid. Yield: 95% (169 mg). Mp: 175-177 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.54 (q, J = 8.6 Hz, 4H), 7.38 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.2, 154.7, 138.1, 132.1, 131.2, 130.8, 129.4, 129.3, 129.2, 127.9, 127.2, 127.1, 126.6, 124.1. ESI-MS m/z (%) 355.90 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{16}H_{10}BrN_3S$ $[MH^+]$: 355.9852; Found: 355.9852.

6-(4-Bromophenyl)-5-(3-methoxyphenyl)thiazolo[3,2-*b*]-1,2,4-triazole (3bb)

Colorless solid. Yield: 92% (178 mg). Mp: 133-135 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.18 (s, 1H), 7.55 (q, J = 8.9 Hz, 4H), 7.31 (d, J = 8.1 Hz, 1H), 6.95-6.88 (m, 3H), 3.75 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.9, 155.3, 154.6, 138.1, 132.0, 131.2, 130.4, 127.7, 127.0, 126.6, 124.2, 121.7, 114.9, 55.3. ESI-MS m/z (%) 385.90 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{17}H_{12}BrN_3OS$ $[MH^+]$: 385.9957; Found: 385.9958.

6-(4-Bromophenyl)-5-(4-fluorophenyl)thiazolo[3,2-*b*]-1,2,4-triazole (3bc)

Colorless solid. Yield: 86% (161 mg). Mp: 148-150 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.53 (q, J = 8.5 Hz, 4H), 7.37-7.33 (m, 2H), 7.09 (t, J = 8.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.2 (J_{CF} = 251.1 Hz), 155.3, 154.5, 138.2, 132.2, 131.3 (J_{CF} = 8.4 Hz), 131.1, 130.1, 127.3, 126.9, 126.6, 126.4, 124.3, 116.6 (J_{CF} = 22.0 Hz), 112.2. ESI-MS m/z (%) 373.90 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{16}H_9BrFN_3S$ $[MH^+]$: 373.9757; Found: 373.9759.

6-(4-Bromophenyl)-5-(4-(trifluoromethyl)phenyl)thiazolo[3,2-*b*]-1,2,4-triazole (3bd)

Colorless solid. Yield: 79% (168 mg). Mp: 196-197 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.22 (s, 1H), 7.63 (q, J = 8.5 Hz, 4H), 7.49 (d, J = 8.5 Hz, 4H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.7, 138.4, 134.6, 132.4, 131.2, 129.6, 128.3,126.3, 126.2, 126.1, 125.8, 125.4, 124.7, 121.8. ESI-MS m/z (%) 423.90 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{17}H_9BrF_3N_3S$ $[MH^+]$: 423.9725; Found: 423.9723.

6-(4-Bromophenyl)-5-*p*-tolylthiazolo[3,2-*b*]-1,2,4-triazole (3be)

Colorless solid. Yield: 90% (167 mg). Mp: 146-148 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.54 (q, J = 8.7 Hz, 4H), 7.25 (d, J = 8.2 Hz, 2H), 7.18 (d, J = 8.2 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.1, 154.5, 139.6, 138.0, 132.1, 131.2, 129.9, 129.2, 128.1, 127.9, 126.8, 123.9, 21.3. ESI-MS m/z (%) 369.95 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{17}H_{12}BrN_3S$ $[MH^+]$: 370.0008; Found: 370.0010.

6-(4-Bromophenyl)-5-(4-methoxyphenyl)thiazolo[3,2-*b*]-1,2,4-triazole (3bf)

Colorless solid. Yield: 91% (176 mg). Mp: 144-146 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.16 (s, 1H), 7.54 (q, J = 8.6 Hz, 4H), 7.29 (d, J = 8.9 Hz, 2H), 6.90 (d, J = 8.9 Hz, 2H), 3.84 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.4, 155.0, 154.4, 138.0, 132.1, 131.1, 130.7, 127.9, 126.8, 126.4, 123.9, 122.9, 114.7, 55.4. ESI-MS m/z (%) 385.95 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{17}H_{12}BrN_3OS$ $[MH^+]$: 385.9957; Found: 385.9958.

5-(4-*t*-butylphenyl)-6-(4-bromophenyl)thiazolo[3,2-*b*]-1,2,4-triazole (3bg)

Colorless solid. Yield: 94% (194 mg). Mp: 168-170 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.55 (q, J = 8.7 Hz, 4H), 7.39 (d, J = 9.1 Hz, 2H), 7.28 (d, J = 9.1 Hz, 2H), 1.34 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.2, 154.2, 152.8, 138.1, 132.1, 131.2, 128.9, 127.8, 126.8, 126.7, 126.2, 124.0, 34.8, 31.2. ESI-MS m/z (%) 412.95 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{20}H_{18}BrN_3S$ $[MH^+]$: 412.0478; Found: 412.0480.

6-(4-Bromophenyl)-5-(2-ethylphenyl)thiazolo[3,2-*b*]-1,2,4-triazole (3bh)

Colorless solid. Yield: 93% (179 mg). Mp: 132-134 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.21 (s, 1H), 7.51-7.45 (m, 4H), 7.43-7.25 (m, 4H), 2.49 (q, J = 7.6 Hz, 2H), 1.04 (t, J = 7.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.3, 155.1, 143.9, 137.8, 131.8, 130.0, 129.1, 127.9, 126.8, 126.5, 123.7, 26.1, 14.8. ESI-MS m/z (%) 383.95 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{18}H_{14}BrN_3S$ $[MH^+]$: 384.0165; Found: 384.0166.

6-(4-Bromophenyl)-5-(2-chlorophenyl)thiazolo[3,2-*b*]-1,2,4-triazole (3bi)

Colorless solid. Yield: 85% (166 mg). Mp: 157-159 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.21 (s, 1H), 7.50 (q, J = 8.6 Hz, 4H), 7.45-7.31 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.6, 155.4, 137.9, 135.0, 133.1, 131.4, 130.2, 129.5, 129.2, 127.5, 126.5, 124.1, 123.9. ESI-MS m/z (%) 389.85 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{16}H_9BrClN_3S$ $[MH^+]$: 389.9462; Found: 389.9463.

6-(4-Bromophenyl)-5-(3-fluorophenyl)thiazolo[3,2-*b*]-1,2,4-triazole (3bj)

Colorless solid. Yield: 80% (150 mg). Mp: 153-155 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.18 (s, 1H), 7.55 (q, J = 8.6 Hz, 4H), 7.37 (q, J = 7.2 Hz, 1H), 7.16-7.06 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.4 (J_{CF} = 248.8 Hz), 155.5, 154.6, 138.2, 132.8, 132.3, 131.2, 131.0 (J_{CF} = 8.6 Hz), 127.7, 126.2, 125.1, 124.5, 116.4 (J_{CF} = 22.0 Hz). ESI-MS m/z (%) 373.90 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{16}H_9BrFN_3S$ $[MH^+]$: 373.9757; Found: 373.9758.

6-(4-Bromophenyl)-5-(naphthalen-1-yl)thiazolo[3,2-*b*]-1,2,4-triazole (3bk)

Colorless solid. Yield: 95% (193 mg). Mp: 204-206 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.27 (s, 1H), 8.00-7.85 (m, 3H), 7.58-7.44 (m, 6H), 7.37-7.30 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.6, 155.3, 137.7, 133.8, 131.9, 131.8, 130.7, 130.2, 130.0, 128.9, 128.7, 127.7, 127.5, 126.7, 126.6, 125.4, 124.9, 123.8. ESI-MS m/z (%) 405.95 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{20}H_{12}BrN_3S$ $[MH^+]$: 406.0008; Found: 406.0008.

5-Phenyl-6-*p*-tolylthiazolo[3,2-*b*]-1,2,4-triazole (3ca)

Colorless solid. Yield: 98% (143 mg). Mp: 187-189 °C. ^{1}H

NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.51 (d, J = 8.1 Hz, 2H), 7.36 (m, 5H), 7.25 (m, 2H), 2.40 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.2, 139.9, 131.4, 129.6, 129.3, 129.1, 128.4, 126.6, 124.8, 21.5. ESI-MS m/z (%) 292.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{17}H_{13}N_3S$ $[MH^+]$: 292.0903; Found: 292.0907.

5-(3-Methoxyphenyl)-6-*p*-tolylthiazolo[3,2-*b*]-1,2,4-triazole (3cb)

Colorless solid. Yield: 96% (154 mg). Mp: 117-119 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.16 (s, 1H), 7.52 (d, J = 8.1 Hz, 2H), 7.29-7.23 (m, 3H), 6.97-6.89 (m, 3H), 3.71 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.8, 155.1, 154.4, 139.9, 132.5, 130.9, 130.1, 129.6, 129.5, 128.8, 128.5, 126.5, 124.8, 121.6, 114.7, 55.2, 21.5. ESI-MS m/z (%) 322.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{18}H_{15}N_3OS$ $[MH^+]$: 322.1009; Found: 322.1013.

5-(4-Fluorophenyl)-6-*p*-tolylthiazolo[3,2-*b*]-1,2,4-triazole (3cc)

Yellow solid. Yield: 91% (141 mg). Mp: 187-189 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.48 (d, J = 8.0 Hz, 2H), 7.38-7.33 (m, 2H), 7.26-7.23 (m, 2H), 7.06 (t, J = 8.5 Hz, 2H), 2.40 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.0 (J_{CF} = 250.4 Hz), 155.2, 154.4, 140.1, 131.2 (J_{CF} = 8.3 Hz), 130.1, 129.7, 129.5, 128.8, 128.5, 127.4, 125.4, 124.5, 116.3 (J_{CF} = 21.9 Hz), 114.1, 21.5. ESI-MS m/z (%) 310.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{17}H_{12}FN_3S$ $[MH^+]$: 310.0809; Found: 310.0813.

5-(4-(Trifluoromethyl)phenyl)-6-*p*-tolylthiazolo[3,2-*b*]-1,2,4-triazole (3cd)

Colorless solid. Yield: 88% (158 mg). Mp: 138-140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.18 (s, 1H), 7.61 (d, J = 8.1 Hz, 2H), 7.49 (d, J = 8.3 Hz, 4H), 7.27 (d, J = 8.1 Hz, 2H), 2.42 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.5, 154.6, 140.5, 135.1, 131.0, 130.6, 129.8, 129.6, 129.5, 126.1, 126.0, 125.5, 124.7, 124.2, 121.9, 114.0, 21.5. ESI-MS m/z (%) 360.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{18}H_{12}F_3N_3S$ $[MH^+]$: 360.0777; Found: 360.0781.

5,6-Di-*p*-tolylthiazolo[3,2-*b*]-1,2,4-triazole (3ce)

Yellow solid. Yield: 92% (140 mg). Mp: 203-205 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.16 (s, 1H), 7.51 (d, J = 8.1 Hz, 2H), 7.25 (dd, J = 10.7, 5.0 Hz, 4H), 7.15 (d, J = 8.1 Hz, 2H), 2.38 (d, J = 7.9 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.1, 139.8, 139.1, 129.8, 129.6, 129.1, 128.4, 128.0, 126.8, 124.9, 114.1, 21.5, 21.3. ESI-MS m/z (%) 306.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{18}H_{15}N_3S$ $[MH^+]$: 306.1059; Found: 306.1062.

5-(4-Methoxyphenyl)-6-*p*-tolylthiazolo[3,2-*b*]-1,2,4-triazole (3cf)

Colorless solid. Yield: 93% (158 mg). Mp: 168-169 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.15 (s, 1H), 7.51 (d, J = 8.5 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 6.88 (d, J = 8.5 Hz, 2H), 3.83 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.1, 155.0, 139.7, 130.6, 129.5, 126.6, 124.9, 123.5, 114.5, 55.0, 21.5. ESI-MS m/z (%) 322.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{18}H_{15}N_3OS$ $[MH^+]$: 322.1009; Found: 322.1012.

5-(4-*t*-butylphenyl)-6-*p*-tolylthiazolo[3,2-*b*]-1,2,4-triazole (3cg)

Colorless solid. Yield: 92% (160 mg). Mp: 119-121 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.15 (s, 1H), 7.52 (d, J = 8.0 Hz, 2H), 7.36 (d, J = 8.5 Hz, 2H), 7.30 (d, J = 8.5 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 2.41 (s, 3H), 1.32 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.1, 154.4, 152.3, 139.8, 129.6, 128.8, 128.3, 127.9, 126.9, 126.0, 125.0, 34.8, 31.2, 21.5. ESI-MS m/z (%) 348.05 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{21}H_{21}N_3S$ $[MH^+]$: 348.1529; Found: 348.1532.

5-(2-Ethylphenyl)-6-*p*-tolylthiazolo[3,2-*b*]-1,2,4-triazole (3ch)

Colorless solid. Yield: 95% (152 mg). Mp: 105-107 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.21 (s, 1H), 7.47 (d, J = 8.2 Hz, 2H), 7.40 (m, 2H), 7.27 (m, 2H), 7.14 (d, J = 8.2 Hz, 2H), 2.49 (q, J = 7.6 Hz, 2H), 2.33 (s, 3H), 1.02 (t, J = 7.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.1, 144.0, 139.5, 132.1, 130.0, 129.6, 129.3, 129.1, 128.5, 126.3, 125.1, 125.0, 26.1, 21.4, 14.8. ESI-MS m/z (%) 320.05 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{19}H_{17}N_3S$ $[MH^+]$: 320.1216; Found: 320.1220.

5-(2-Chlorophenyl)-6-*p*-tolylthiazolo[3,2-*b*]-1,2,4-triazole (3ci)

Colorless solid. Yield: 88% (143 mg). Mp: 125-127 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.21 (s, 1H), 7.50-7.36 (m, 5H), 7.31 (dd, J = 7.4, 1.3 Hz, 1H), 7.17 (d, J = 8.0 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.6, 155.3, 139.8, 135.1, 133.3, 131.0, 130.5, 130.3, 130.0, 129.4, 128.7, 127.3, 124.7, 124.0, 122.6, 114.1, 21.4. ESI-MS m/z (%) 326.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{17}H_{12}ClN_3S$ $[MH^+]$: 326.0513; Found: 326.0517.

5-(3-Fluorophenyl)-6-*p*-tolylthiazolo[3,2-*b*]-1,2,4-triazole (3cj)

Colorless solid. Yield: 83% (128 mg). Mp: 148-150 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.49 (d, J = 8.6 Hz, 2H), 7.37-7.25 (m, 3H), 7.16 (d, J = 6.9 Hz, 1H), 7.07 (d, J = 8.6 Hz, 2H), 2.41 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.8 (J_{CF} = 248.1 Hz), 155.4, 154.6, 140.4, 133.5, 133.4, 130.8 (J_{CF} = 8.2 Hz), 129.8, 129.6, 129.1, 125.0, 124.4, 116.2 (J_{CF} = 21.9 Hz), 21.5. ESI-MS m/z (%) 310.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{17}H_{12}FN_3S$ $[MH^+]$: 310.0809; Found: 310.0813.

5-(Naphthalen-1-yl)-6-*p*-tolylthiazolo[3,2-*b*]-1,2,4-triazole (3ck)

Colorless solid. Yield: 96% (164 mg). Mp: 142-144 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.25 (s, 1H), 7.96-7.90 (m, 3H), 7.59-7.44 (m, 6H), 7.03 (d, J = 7.9 Hz, 2H), 2.26 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.6, 155.2, 139.5, 133.7, 132.2, 130.3, 129.2, 128.6, 128.3, 127.2, 126.5,, 125.4, 125.2, 124.8, 124.5, 124.0, 119.1, 114.1, 21.3. ESI-MS m/z (%) 342.05 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{21}H_{15}N_3S$ $[MH^+]$: 342.1059; Found: 342.1065.

6-Methyl-5-phenylthiazolo[3,2-*b*]-1,2,4-triazole (3da)

Colorless oil. Yield: 90% (97 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.50-7.42 (m, 5H), 2.64 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.2, 154.5, 131.1, 130.9, 129.1, 129.0, 128.9, 125.6, 125.1, 114.1, 11.7. ESI-MS m/z (%) 216.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{11}H_9N_3S$ $[MH^+]$: 216.0590; Found: 216.0591.

5-(3-Methoxyphenyl)-6-methylthiazolo[3,2-*b*]-1,2,4-triazole (3db)

Colorless solid. Yield: 98% (120 mg). Mp: 105-106 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.18 (s, 1H), 7.41 (t, J = 7.9 Hz, 1H),

7.07 (d, J = 7.5 Hz, 1H), 6.99 (d, J = 9.6 Hz, 2H), 3.87 (s, 3H), 2.66 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.0, 155.3, 132.3, 130.3, 125.4, 125.3, 121.4, 114.9, 114.3, 114.1, 55.4, 11.8. ESI-MS m/z (%) 246.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{12}H_{11}N_3OS$ $[MH^+]$: 246.0696; Found: 246.0698.

5-(4-Fluorophenyl)-6-methylthiazolo[3,2-*b*]-1,2,4-triazole (3dc)

Colorless solid. Yield: 83% (97 mg). Mp: 94-96 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.49-7.45 (m, 2H), 7.20 (t, J = 8.5 Hz, 2H), 2.61 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.0 (J_{CF} = 250.2 Hz), 155.2, 154.3, 131.0 (J_{CF} = 8.4 Hz), 127.1, 125.3, 124.4, 116.3 (J_{CF} = 21.9 Hz), 11.5. ESI-MS m/z (%) 234.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{11}H_8FN_3S$ $[MH^+]$: 234.0496; Found: 234.0495.

5-(4-(Trifluoromethyl)phenyl)-6-methylthiazolo[3,2-*b*]-1,2,4-triazole (3dd)

Colorless solid. Yield: 76% (108 mg). Mp: 120-122 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.20 (s, 1H), 7.77 (d, J = 8.2 Hz, 2H), 7.62 (d, J = 8.2 Hz, 2H), 2.68 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.7, 134.8, 131.2, 130.7, 129.3, 126.3, 126.2, 126.1, 123.9, 122.0, 114.1, 11.8. ESI-MS m/z (%) 284.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{12}H_8F_3N_3S$ $[MH^+]$: 284.0464; Found: 284.0468.

6-Methyl-5-p-tolylthiazolo[3,2-*b*]-1,2,4-triazole (3de)

Colorless solid. Yield: 93% (107 mg). Mp: 103-105 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.38 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 2.63 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.2, 139.1, 129.8, 128.9, 128.0, 125.7, 124.4, 123.5, 114.1, 21.3, 11.7. ESI-MS m/z (%) 230.00 (100) $[M+H]^+$. ESI-MS m/z (%) 284.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{12}H_{11}N_3S$ $[MH^+]$: 230.0746; Found: 230.0748.

5-(4-Methoxyphenyl)-6-methylthiazolo[3,2-*b*]-1,2,4-triazole (3df)

Colorless solid. Yield: 92% (113 mg). Mp: 102-104 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.16 (s, 1H), 7.41 (d, J = 8.7 Hz, 2H), 7.01 (d, J = 8.7 Hz, 2H), 3.88 (s, 3H), 2.61 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.1, 155.1, 139.3, 130.4, 125.5, 124.4, 123.5, 123.3, 114.6, 55.4, 11.6. ESI-MS m/z (%) 246.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{12}H_{11}N_3OS$ $[MH^+]$: 246.0696; Found: 246.0699.

5-(4-*t*-butylphenyl)-6-methylthiazolo[3,2-*b*]-1,2,4-triazole (3dg)

Colorless solid. Yield: 99% (134 mg). Mp: 109-111 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.51 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 8.4 Hz, 2H), 2.65 (s, 3H), 1.37 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.2, 152.2, 128.7, 128.2, 126.1, 125.7, 124.8, 114.1, 34.8, 31.2, 11.7. ESI-MS m/z (%) 272.00 (74) $[M+H]^+$. HRMS (ESI) calcd. for $C_{15}H_{17}N_3S$ $[MH^+]$: 272.1216; Found: 272.1218.

5-(2-Ethylphenyl)-6-methylthiazolo[3,2-*b*]-1,2,4-triazole (3dh)

Colorless oil. Yield: 94% (114 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.18 (s, 1H), 7.46-7.36 (m, 2H), 7.31 (t, J = 7.1 Hz, 2H), 2.64 (q, J = 7.5 Hz, 2H), 2.38 (s, 3H), 1.17 (t, J = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.1, 144.6, 131.9, 130.1, 129.0, 128.7, 126.1, 124.0, 114.1, 26.3, 15.4, 11.2. ESI-MS m/z (%) 244.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{13}H_{13}N_3S$ $[MH^+]$: 244.0903; Found: 244.0907.

5-(2-Chlorophenyl)-6-methylthiazolo[3,2-*b*]-1,2,4-triazole (3di)

Colorless oil. Yield: 87% (109 mg). ^{1}H NMR (300 MHz, $CDCl_3$):δ 8.18 (s, 1H), 7.55 (d, J = 8.3 Hz, 1H), 7.47-7.35 (m, 3H), 2.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.3, 135.1, 133.0, 131.1, 130.3, 129.2, 127.5, 127.2, 121.7, 114.1, 11.6. ESI-MS m/z (%) 249.95 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{11}H_8ClN_3S$ $[MH^+]$: 250.0200; Found: 250.0202.

5-(3-Fluorophenyl)-6-methylthiazolo[3,2-*b*]-1,2,4-triazole (3dj)

Colorless solid. Yield: 81% (94 mg). Mp: 114-116 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.18 (s, 1H), 7.51-7.44 (m, 1H), 7.29-7.12 (m, 3H), 2.66 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.9 (J_{CF} = 248.4 Hz), 155.4, 154.4, 130.9 (J_{CF} = 8.6 Hz), 125.8, 124.8, 116.2, 116.0 (J_{CF} = 22.0 Hz), 114.1, 11.7. ESI-MS m/z (%) 234.00 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{11}H_8FN_3S$ $[MH^+]$: 234.0496; Found: 234.0499.

6-Methyl-5-(naphthalen-1-yl)thiazolo[3,2-*b*]-1,2,4-triazole (3dk)

Yellow oil. Yield: 93% (123 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.23 (s, 1H), 8.02-7.95 (m, 2H), 7.86 (d, J = 9.2 Hz, 1H), 7.62-7.55 (m, 4H), 2.40 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.4, 155.2, 133.7, 132.2, 130.3, 130.0, 128.7, 127.5, 127.3, 127.1, 126.6, 125.2, 125.0, 122.8, 114.1, 11.6. ESI-MS m/z (%) 266.05 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{15}H_{11}N_3S$ $[MH^+]$: 266.0746; Found: 266.0748.

6-Methyl-5-D_5-phenylthiazolo[3,2-*b*]-1,2,4-triazole (5)

Colorless solid. Yield: 88% (97 mg). Mp: 82-83 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H), 2.64 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.2, 130.9, 128.9, 128.8, 128.4, 128.3, 128.1, 125.4, 125.0, 114.1, 11.7. ESI-MS m/z (%) 221.05 (100) $[M+H]^+$. HRMS (ESI) calcd. for $C_{11}H_4D_5N_3S$ $[MH^+]$: 221.0904; Found: 221.0906.

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