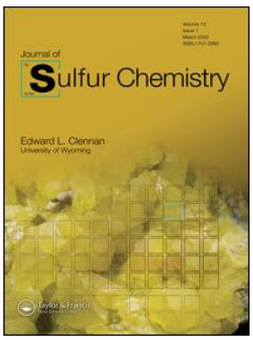

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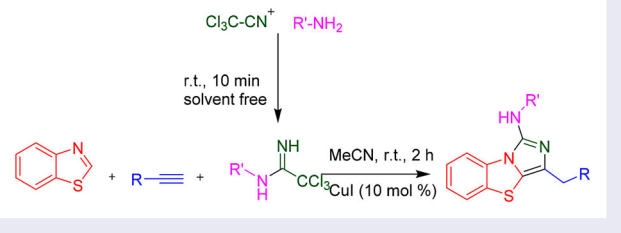
A new route for the synthesis of functionalized benzo[d]imidazo[5,1-b]thiazol-1-amine derivatives from benzothiazole, trichloroacetamidines and terminal alkynes

Maryam Bayanati[a], Niloofar Parizadeh[b], Manijeh Nematpour[a], Anna Sedaghat[c] and Sayyed Abbas Tabatabaia[a]

[a]Department of Pharmaceutical Chemistry, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [b]Faculty of Chemistry, Institute of Organic Chemistry, University of Vienna, Vienna, Austria; [c]Student Research Committee, (Department and Faculty of pharmacy), Shahid Beheshti University of Medical Sciences, Tehran, Iran

ABSTRACT

A novel class of substituted benzo[d]imidazo[5,1-b]thiazol-1-amine derivatives was synthesized utilizing a one-pot Cu-catalyzed cycloaddition of benzothiazole, trichloroacetonitrile, various amines and terminal alkynes in acetonitrile at room temperature. The speed of this simple four-component reaction along with mild conditions, high yields, readily available starting materials, the ease of work-up without using pollutant precious metals–catalysts, and column chromatography are important features of the presented procedure.



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Benzo[d]imidazo[5,1-b]thiazol-1-amine; C-H Activation; Cu-catalyzed; One-pot

1. Introduction

These Sulfur-containing heterocycles commonly exist and are isolated from natural products, and their various biological and pharmaceutical applications have attracted much attention [1–4]. Benzo-thiazolo-imidazole is a fuzed tricyclic sulfur-containing heterocycle and valuable building block with biological activity ranging from antineoplastic [5,6], antibacterial [7–10], to labeled molecules as an excellent fluoroprobe for PET scan analysis of Alzheimer disease (see Figure 1) [11–13].

CONTACT Sayyed Abbas Tabatabaia sa_tabatabai@sbmu.ac.ir

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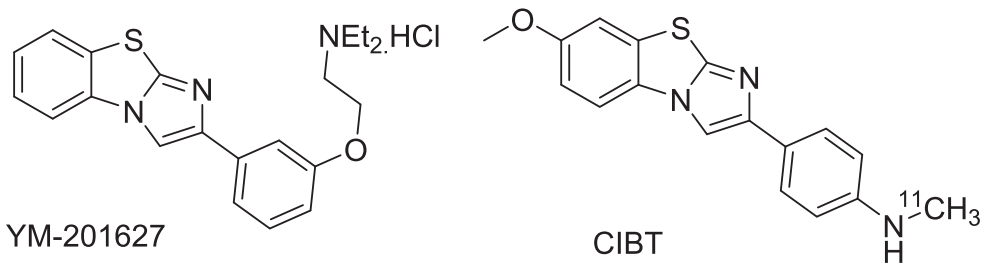
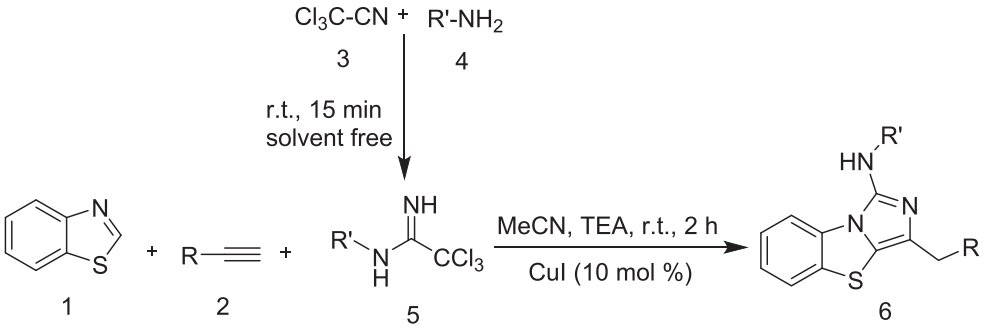


Figure 1. YM-201627 (anti-cancer) and CIBT (PET tracer) with benzothiazolo-imidazole core.



Scheme 1. Synthesis of various benzo-thiazolo-imidazole derivatives.

The less and costly available materials, low yields, complicated workup, and toxic catalysts still limits the synthesis of this scaffold [14–17]. Therefore, an efficient simple method to synthesize this scaffold is still ongoing [18–22]. Cu-catalyzed C-H activation is a remarkable method for preparing heterocyclic compounds [23,24]. Various multi-component reactions (MCRs) using copper- a catalyst for creating new heterocyclic compounds have been previously reported by our research group [25–29].

Continuing our previous work and given the importance of substituted benzo[*d*] imidazo[*5,1-b*]thiazol-1-amine derivatives, we developed a highly efficient method copper-catalyzed synthesis, one-pot four-component reaction of benzothiazole **1**, terminal alkynes **2**, trichloroacetonitrile **3** and various amines **4**. In practice, the experiments were carried out using *in situ* preparation of trichloroacetamidines intermediate **5** from the reaction of

trichloroacetonitrile **3** and various amines **4.** The electron-withdrawing effect of the -CCl_3 makes the nitrile group of trichloroacetonitrile prone to the attack of nucleophilic amine (see Scheme 1).

2. Results and discussion

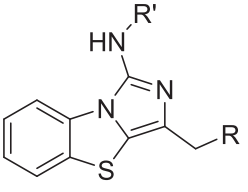
The reaction conditions optimization were done using phenylacetylene (1.0 mmol), benzothiazole (1.5 mmol), trichloroacetonitrile (1.0 mmol) and benzylamine (1.5 mmol) as a model of precursors. Copper and a few of its salts and various solvents were investigated to optimize the reaction. The best results were obtained using 10 mol % of cuprous iodide (CuI) as catalyst and acetonitrile (MeCN) as solvent respectively. This optimal catalytic

Table 1. Optimization of reaction conditions for the formation of product **6a** from 1.5 mmol of benzylamine, 1.5 mmol of benzothiazole, 1.0 mmol of phenylacetylene, 1.0 mmol of trichloroacetonitrile, 10 mol % of copper salt as the catalyst and 1.0 mmol of the TEA at room temperature.

Entry	Catalyst	Solvent	Yield (%)[a]
1[b]	CuI	MeCN	88
2	CuI	DMSO	32
3	CuI	DMF	22
4	CuI	THF	70
5	CuCl	MeCN	70
6	CuCl	Toluene	30
7	CuBr	MeCN	54
8	CuBr	THF	42
9	CuBr	DMF	16
10	$Cu(OAc)_2$	MeCN	16
11	Cu	THF	-
12	Cu	MeCN	-

[a] Reaction time 2 h.
[b] 5 mol% catalyst, reaction time was 5 h.

Table 2. Synthesis of various benzo[*d*]imidazo[*5,1-b*]thiazol-1-amine derivatives.

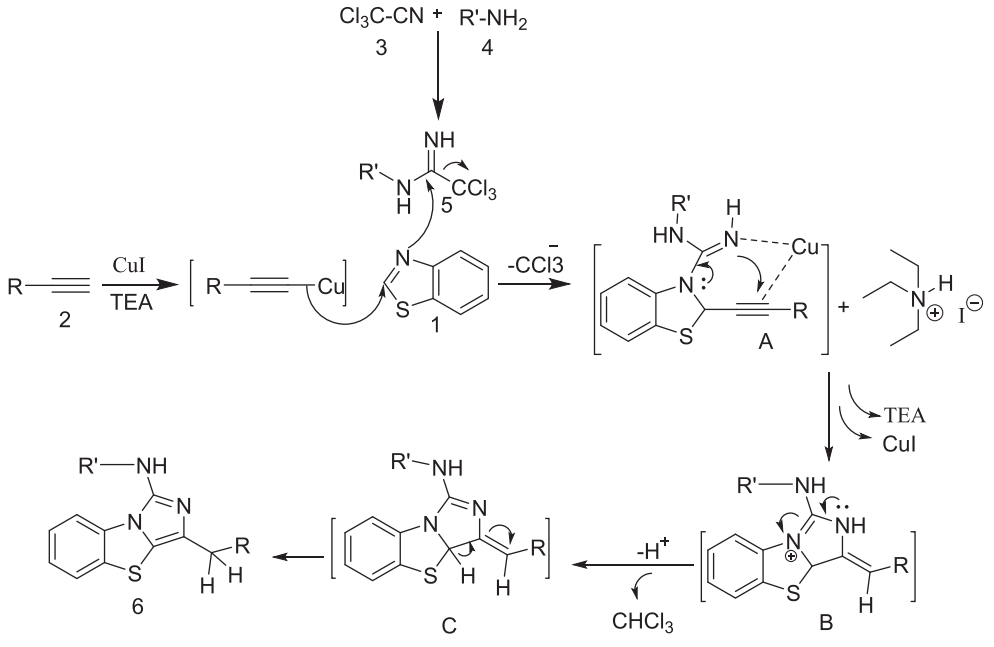


6 (a-l)

Compound	R	R′	Yield (%)
6a	Ph	Ph-CH_2	88
6b	Ph	4-Me-C_6H_4-CH_2	85
6c	Ph	4-OMe-C_6H_4-CH_2	79
6d	Ph	4-F-C_6H_4-CH_2	90
6e	Ph	Ph	81
6f	Ph	4-Me-C_6H_4	80
6g	Ph	4-OMe-C_6H_4	78
6h	Ph	4-F-C_6H_4	82
6i	Pr	4-F-C_6H_4-CH_2	76
6j	Pr	4-Me-C_6H_4-CH_2	77
K	Bu	4-F-C_6H_4-CH_2	80
l	Bu	4-Me-C_6H_4-CH_2	83

effect of CuI is probably due to its more solubility in the solvent. The experiments have shown that the use of 1.0 mmol of triethylamine as a base significantly accelerates the reaction rate. The optimization results are summarized in Table 1.

Finally, twelve analogs of benzo[*d*]imidazo[*5,1-b*]thiazol-1-amine derivatives were synthesized from benzothiazole, trichloroacetonitrile, terminal alkynes and amines with a diversity of substituents (electron-withdrawing or electron-donating) on the aromatic rings (see Table 2).



Scheme 2. Plausible formation mechanism of compounds **6**.

The structural spectra of final product **6a-6l** were assigned using Infrared, ^{1}H NMR, ^{13}C NMR, and mass spectroscopy. As an example, the ^{1}H NMR spectrum of compound **6a**, displayed a singlet signal for the NH group ($\delta_H = 5.21$ ppm) and two singlet peaks for methylene groups ($\delta_H = 3.04$ and 3.55 ppm). Also, characteristic multiplet signals for the phenyl protons were seen in the aromatic zone. The ^{13}C NMR spectrum of **6a** displayed 16 signals in accordance with the desired structure. The mass spectrum of compound **6a** showed a signal of molecular ion at m/z = 369. The NMR spectra of compounds **6b-l** were similar to those of **6a** and exhibited corresponding signals due to structural differences.

A plausible mechanism for the formation of compounds **6** is shown in Scheme 2. Initially, the nucleophilic addition of amine **4** to trichloroacetonitrile **3** leads to the formation of trichloromethylamidine adduct **5** which is susceptible to a substitution by negatively charged nitrogen of benzothiazole to leave CCl_3 group. In practice, negatively charged nitrogen can be produced by the attack of *in situ* prepared corresponding copper acetylide intermediate (CuC≡CR) to number 2 carbon of the benzothiazole ring. The six-membered complex **A** resulting from the coordination of copper with a triple bond of substituted acetylene and NH group facilitates the ring formation. Finally, product **6** is formed upon the tautomerization of the intermediates **C** to create an aromatic imidazole ring. The absence of halogen to facilitate ring formation makes our method distinct from the hybrid of alkyne hydroamination / Heck reaction. The uptake of protons in the reaction medium by TEA probably contributes to the improvement of the reaction.

3. Conclusion

In conclusion, we have developed a simple CuI-catalyzed one-pot four-component reaction involving trichloroacetonitrile, benzothiazole, terminal acetylene, and various amines.

This novel method involves the formation of three new C–N bonds in an intermolecular cycloaddition reaction for efficient synthesizing benzo[*d*]imidazo[*5,1-b*]thiazol-1-amine derivatives. The present work introduces an excellent alternative over earlier methods in terms of high yields, operational simplicity, availability of raw materials, and mild conditions.

4. Experimental

All chemicals were used without further purification and provided from Merck company. Melting points (m.p), IR spectra, and CHN Elemental analyses were carried out using an Electrothermal 9100 apparatus, Shimadzu IR-460 spectrometer, and Heraeus CHN-O-Rapid analyzer, respectively. The melting points are uncorrected. *Finnigan-MAT-8430EI-MS,* was adjusted to achieve mass spectrometer; at 70 eV; in *m/z* (rel. %). 1H and 13C NMR spectra were recorded by *Bruker DRX-500 Avance* instrument, TMS as internal standard, and $CDCl_3$ as tested solvent at 500.1 and 125.7 MHz, respectivley. The abbreviations applied for NMR signals: s = singlet, d = doublet, t = triplet, m = multiplet, and δ in ppm, J in Hz.

4.1. General procedure for preparation of compounds 6

Trichloroacetonitrile **3** (1.0 mmol) and appropriate amine **4** (1.5 mmol) were reacted exothermically under a neat condition for 15 min at 25°C. Then, benzothiazole **1** (1.5 mmol), substituted acetylene **2** (1.0 mmol), CuI (0.1 mmol), and TEA (1.0 mmol) were mixed in acetonitrile (3 ml). Then after, it was added slowly to the primary reaction, and stirring is continued for 2 h. The reaction progress is monitored using thin-layer chromatography (ethyl acetate/hexane 1:3). The mixture was diluted with 2.0 mL of $CHCl_3$ and then was shaken well twice with 2.0 mL saturated aqueous solution of NH_4Cl to remove CuI. The organic fraction was dried over anhydrous sodium sulfate, and then filtered off, and the solvent was evaporated under reduced pressure, and crude solid was washed with normal hexane to afford the pure product.

***N*, 3-Dibenzylbenzo[*d*]imidazo[*5,1-b*]thiazol-1-amine (6a):** White powder; yield: 0.32 g (88%); mp: 144–147°C. IR (KBr) (ν_{max}, cm^{-1}): 3312, 1640, 1601, 1161. ^{1}H-NMR (500 MHz, $CDCl_3$): δ_H = 3.04 (s, 2 H, CH_2), 3.55 (s, 2 H, CH_2), 5.21 (s, 1 H, NH), 7.19 (d, ^3J = 7.6, 2 H, Ar), 7.23 (t, ^3J = 7.7, 1 H, Ar), 7.27–7.33 (m, 7 H, Ar), 7.45 (d, ^3J = 7.7, 2 H, Ar), 7.47 (d, ^3J = 7.9, 1 H, Ar), 7.88 (d, ^3J = 7.9, 1 H, Ar). ^{13}C-NMR (125.7 MHz, $CDCl_3$): δ_C = 33.0 (CH2), 42.3 (CH2), 126.1 (2CH), 126.7 (2 CH), 127.4 (2 CH), 127.7 (CH), 128.7 (2CH), 129.2 (C), 130.0 (2CH), 132.5 (2CH), 132.9 (2CH), 133.0 (CH), 142.1 (C), 147.3 (C), 153.4 (C), 164.4 (C). MS: m/z (%) = 369 (M^+, 4), 292 (21), 278 (39), 263 (11), 106 (73), 91 (55), 77 (100). Anal. Calc. for $C_{23}H_{19}N_3S$ (369.48): C, 74.77; H, 5.18; N, 11.37%. Found: C, 74.72; H, 5.15; N, 11.39%.

Benzyl-*N*-(4-methylbenzyl)benzo[*d*]imidazo[*5,1-b*]thiazol-1-amine (6b): White powder; yield: 0.34 g (85%); mp: 135–137°C. IR (KBr) (ν_{max}, cm^{-1}): 3318, 1641, 1600, 1151. ^{1}H-NMR (500 MHz, $CDCl_3$): δ_H = 2.09 (s, 3 H, Me), 3.02 (s, 2 H, CH_2), 3.66 (s, 2 H, CH_2), 5.00 (s, 1 H, NH), 7.17 (d, ^3J = 7.7, 2 H, Ar), 7.24 (t, ^3J = 7.7, 2 H, Ar), 7.28–7.31 (m, 3 H, Ar), 7.43 (t, ^3J = 7.8, 1 H, Ar), 7.58 (d, ^3J = 7.8, 2 H, Ar), 7.60 (t, ^3J = 7.9, 1 H,

Ar), 7.87 (d, ^3J = 7.9, 1 H, Ar), 8.01 (d, ^3J = 7.9, 1 H, Ar). ^{13}C-NMR (125.7 MHz, $CDCl_3$): δ_C = 24.1 (Me), 34.4CH_2), 41.2 (CH_2), 126.2 (2 CH), 126.6 (C), 127.3 (2 CH), 127.8 (CH), 128.7 (2 CH), 130.0 (CH), 130.7 (2 CH), 131.7 (2 CH), 132.5 (CH), 135.7 (C), 136.6 (C), 144.7 (C), 152.4 (C), 153.4 (C), 163.2 (C), 165.7 (C). MS: m/z (%) = 383 (M^+, 2), 306 (22), 292 (29), 334 (37), 263 (100), 120 (33), 91 (50), 77 (40). Anal. Calc. for $C_{24}H_{21}N_3S$ (383.51): C, 75.16; H, 5.52; N, 10.96%. Found: C, 75.12; H, 5.50; N, 10.94%.

Benzyl-*N*-(4-methoxybenzyl)benzo[*d*]imidazo[*5,1-b*]thiazol-1-aminee (6c): Cream powder; yield: 0.37 g (79%); mp: 148–150°C. IR (KBr) (ν_{max}, cm^{-1}): 3300, 1643, 1600, 1198. ^{1}H-NMR (500 MHz, $CDCl_3$): δ_H = 2.46 (s, 2 H, CH_2), 3.07 (s, 2 H, CH_2), 4.12 (s, 3 H, OMe), 5.11 (s, 1 H, NH), 7.10 (d, ^3J = 7.7, 2 H, Ar), 7.27 (t, ^3J = 7.7, 1 H, Ar), 7.28–7.35 (m, 6 H, Ar), 7.38 (d, ^3J = 7.7, 2 H, Ar), 7.50 (d, ^3J = 7.9, 1 H, Ar), 7.88 (d, ^3J = 7.9, 1 H, Ar). ^{13}C-NMR (125.7 MHz, $CDCl_3$): δ_C = 33.2 (CH_2), 47.8 (CH_2), 57.4 (OMe), 126.8 (2 CH), 127.5 (C), 128.7 (2 CH), 129.8 (CH), 130.0 (2 CH), 132.8 (2 CH), 132.9 (2 CH), 132.5 (2 CH), 136.7 (C), 141.1 (C), 147.9 (C), 153.1 (C), 154.8 (C), 164.2 (C), 166.8 (C).MS: m/z (%) = 399 (M^+, 2), 322 (21), 292 (38), 278 (35), 121 (33), 107 (36), 91 (100), 77 (61). Anal. Calc. for $C_{24}H_{21}N_3OS$ (399.51): C, 72.15; H, 5.30; N, 10.52%. Found: C, 72.12; H, 5.34; N, 10.57%.

Benzyl-*N*-(4-fluorobenzyl)benzo[*d*]imidazo[*5,1-b*]thiazol-1-amine (6d): Cream powder; yield: 0.34 g (90%); mp: 182–185°C. IR (KBr) (ν_{max}, cm^{-1}): 3167, 1621, 1600, 1155. ^{1}H-NMR (500 MHz, $CDCl_3$): δ_H = 3.02 (s, 2 H, CH_2), 3.65 (s, 2 H, CH_2), 5.24 (s, 1 H, NH), 7.20 (d, ^3J = 7.7, 2 H, Ar), 7.25 (t, ^3J = 7.7, 2 H, Ar), 7.25–7.30 (m, 7 H, Ar), 7.47 (d, ^3J = 7.9, 1 H, Ar), 8.13 (d, ^3J = 7.9, 1 H, Ar). ^{13}C-NMR (125.7 MHz, $CDCl_3$): δ_C = 32.8(CH_2), 41.8 (CH_2), 126.1 (2 CH), 128.7 (CH), 129.2 (2 CH), 130.0 (CH), 131.6 (CH), 131.9 (C), 132.5 (2 CH), 132.9 (2 CH), 133.0 (C), 134.1 (CH), 135.7 (CH), 140.1 (C), 141.2 (C), 152.5 (C), 154.2 (C), 162.2 (C), 165.6 (C).MS: m/z (%) = 387 (M^+, 2), 310 (44), 296 (22), 292 (29), 95 (100), 91 (51), 77 (42). Anal. Calc. for $C_{23}H_{18}FN_3S$ (387.47): C, 71.29; H, 4.68; N, 10.84%. Found: C, 71.25; H, 4.62; N, 10.89%.

Benzyl-*N*-phenylbenzo[*d*]imidazo[*5,1-b*]thiazol-1-amine (6e): White powder; yield: 0.31 g (81%); mp: 172–175°C. IR (KBr) (ν_{max}, cm^{-1}): 3189, 1643, 1591, 1160. ^{1}H-NMR (500 MHz, $CDCl_3$): δ_H = 3.11 (s, 2 H, CH_2), 5.89 (s, 1 H, NH), 7.17 (d, ^3J = 7.6, 2 H, Ar), 7.24 (t, ^3J = 7.7, 1 H, Ar), 7.31–7.36 (m, 5 H, Ar), 7.49 (d, ^3J = 7.7, 2 H, Ar), 7.59 (d, ^3J = 7.9, 1 H, Ar), 7.78 (d, ^3J = 7.9, 1 H, Ar), 8.00 (d, ^3J = 7.7, 2 H, Ar). ^{13}C-NMR (125.7 MHz, $CDCl_3$): δ_C = 34.7 (CH_2), 126.9 (2 CH), 127.4 (2 CH), 127.8 (CH), 128.8 (2 CH), 130.0 (C), 130.2 (CH), 130.8 (2 CH), 131.7 (2 CH), 132.9 (2 CH), 135.8 (C), 144.7 (C), 147.3 (C), 152.9 (C), 154.5 (C), 165.9 (C). MS: m/z (%) = 355 (M^+, 9), 278 (44), 264 (10), 263 (21), 91 (100), 77 (65). Anal. Calc. for $C_{22}H_{17}N_3S$ (355.46): C, 74.34; H, 4.82; N, 11.82%. Found: C, 74.42; H, 4.84; N, 11.87%.

Benzyl-*N*-(*p*-tolyl)benzo[*d*]imidazo[*5,1-b*]thiazol-1-amine (6f): Cream powder; yield: 0.33 g (80%); mp: 162–165°C. IR (KBr) (ν_{max}, cm^{-1}):3219, 1623, 1590, 1135. ^{1}H-NMR (500 MHz, $CDCl_3$): δ_H = 2.22 (s, 3 H, Me), 2.56 (s, 2 H, CH_2), 5.87 (s, 1 H, NH), 7.30–7.35 (m, 7 H, Ar), 7.47–7.51 (m, 4 H, Ar), 7.59 (t, ^3J = 7.7, 1 H, Ar), 7.98 (d, ^3J = 7.9, 1 H, Ar). ^{13}C-NMR (125.7 MHz, $CDCl_3$): δ_C = 30.0 (Me), 35.0 (CH_2), 128.8 (2 CH), 129.2 (2 CH), 129.3 (C), 129.4 (2 CH), 130.3 (2 CH), 130.8 (CH), 131.8 (2 CH), 132.5 (CH), 134.3 (CH), 134.4 (CH), 134.9 (C), 135.0 (C), 144.7 (C), 153.4 (C), 164.5 (C), 167.9 (C). MS: m/z

(%) = 369 (M^+, 8), 292 (33), 278 (10), 106 (21), 91 (50), 77 (68). Anal. Calc. for $C_{23}H_{19}N_3S$ (369.48): C, 74.77; H, 5.18; N, 11.37%. Found: C, 74.72; H, 5.14; N, 11.34%.

Benzyl-*N*-(4-methoxyphenyl)benzo[*d*]imidazo[*5,1-b*]thiazol-1-amine(6g): White powder; yield: 0.35 g (78%); mp: 165–167°C. IR (KBr) (ν_{max}, cm^{-1}): 3299, 1641, 1590, 1129. ^{1}H-NMR (500 MHz, $CDCl_3$): δ_H = 2.93 (s, 2 H, CH_2), 4.13 (s, 3 H, OMe), 5.99 (s, 1 H, NH), 7.19 (d, ^3J = 7.7, 2 H, Ar), 7.22 (t, ^3J = 7.7, 1 H, Ar), 7.24–7.32 (m, 6 H, Ar), 7.38 (d, ^3J = 7.7, 2 H, Ar), 7.47 (d, ^3J = 7.9, 1 H, Ar), 7.88 (d, ^3J = 7.9, 1 H, Ar). ^{13}C-NMR (125.7 MHz, $CDCl_3$): δ_C = 33.0 (CH_2), 56.6 (OMe), 126.1 (2 CH), 126.7 (2 CH), 127.4 (2 CH), 127.8 (CH), 128.7 (2 CH), 129.2 (CH), 129.5 (C), 130.0 (2 CH), 130.6 (2 CH), 132.5 (C), 142.1 (C), 147.3 (C), 150.2 (C), 160.1 (C), 164.3 (C). MS: m/z (%) = 385 (M^+, 8), 308 (22), 278 (55), 263 (20), 122 (33), 107 (100), 91 (50), 77 (66). Anal. Calc. for $C_{23}H_{19}N_3OS$ (385.48): C, 71.66; H, 4.97; N, 10.90%. Found: C, 71.62; H, 4.94; N, 10.91%.

Benzyl-*N*-(4-fluorophenyl)benzo[*d*]imidazo[*5,1-b*]thiazol-1-amine (6h): Cream powder; yield: 0.31 g (82%); mp: 181–184°C. IR (KBr) (ν_{max}, cm^{-1}): 3189, 1629, 1600, 1134. ^{1}H-NMR (500 MHz, $CDCl_3$): δ_H = 2.01 (s, 2 H, CH_2), 6.00 (s, 1 H, NH), 7.18 (d, ^3J = 7.6, 2 H, Ar), 7.23 (t, ^3J = 7.7, 1 H, Ar), 7.24–7.31 (m, 4 H, Ar), 7.43 (d, ^3J = 7.7, 2 H, Ar), 7.58 (t, ^3J = 7.9, 2 H, Ar), 7.60 (d, ^3J = 7.9, 1 H, Ar), 8.00 (d, ^3J = 7.7, 1 H, Ar). ^{13}C-NMR (125.7 MHz, $CDCl_3$): δ_C = 32.9 (CH_2), 127.3 (2 CH), 127.8 (2 CH), 128.7 (2 CH), 128.9 (C), 129.2 (2 CH), 130.0 (2 CH), 130.1 (2 CH), 132.9 (CH), 135.7 (C), 136.8 (C), 144.7 (C), 147.3 (C), 154.2 (C), 159.5 (C), 165.9 (C).MS: m/z (%) = 373 (M^+, 10), 296 (15), 282 (18), 278 (74), 95 (100), 91 (50), 77 (61). Anal. Calc. for $C_{22}H_{16}FN_3S$ (373.45): C, 70.76; H, 4.32; N, 11.25%. Found: C, 70.73; H, 4.30; N, 11.27%.

Butyl-*N*-(4-fluorobenzyl)benzo[*d*]imidazo[*5,1-b*]thiazol-1-amine (6i): White powder; yield: 0.29 g (76%); mp: 122–125°C. IR (KBr) (ν_{max}, cm^{-1}):3212, 1699, 1593, 1188. ^{1}H-NMR (500 MHz, $CDCl_3$): δ_H = 0.88 (3 H, t, ^3J = 6.7 Hz, Me), 1.38–1.40 (2 H, m, CH_2), 1.46–1.49 (2 H, m, CH_2), 2.14 (2 H, t, ^3J = 6.7 Hz, CH_2), 3.10 (s, 2 H, CH_2), 5.09 (s, 1 H, NH), 7.19 (d, ^3J = 7.8, 2 H, Ar), 7.25 (t, ^3J = 7.9, 1 H, Ar), 7.33 (t, ^3J = 7.9, 1 H, Ar), 7.60 (d, ^3J = 7.9, 1 H, Ar), 7.72 (d, ^3J = 7.9, 1 H, Ar), 8.01 (d, ^3J = 7.8, 2 H, Ar). ^{13}C-NMR (125.7 MHz, $CDCl_3$): δ_C = 14.0 (Me), 18.4 (CH_2), 20.9 (CH_2), 22.2 (CH_2), 40.0 (CH_2), 126.1 (2 CH), 127.3 (2 CH), 127.7 (CH), 128.9 (C), 129.9 (CH), 130.1 (CH), 131.8 (CH), 135.7 (C), 144.8 (C), 152.7 (C), 153.8 (C), 162.2 (C), 165.0 (C). MS: m/z (%) = 353 (M^+, 2), 296 (20), 258 (19), 244 (61), 110 (100), 95 (51), 57 (97). Anal. Calc. for $C_{20}H_{20}FN_3S$ (353.46): C, 67.96; H, 5.70; N, 11.89%. Found: C, 67.91; H, 5.73; N, 11.83%.

Butyl-*N*-(4-methylbenzyl)benzo[*d*]imidazo[*5,1-b*]thiazol-1-amine (6j): Cream powder; yield: 0.29 g (77%); mp: 112–115°C. IR (KBr) (ν_{max}, cm^{-1}): 3111, 1649, 1591, 1121. ^{1}H-NMR (500 MHz, $CDCl_3$): δ_H = 0.87 (3 H, t, ^3J = 6.7 Hz, Me), 1.37–1.40 (2 H, m, CH_2), 1.45–1.47 (2 H, m, CH_2), 1.90 (2 H, t, ^3J = 6.7 Hz, CH_2), 2.44 (s, 3 H, Me), 2.92 (s, 2 H, CH_2), 5.11 (s, 1 H, NH), 7.16–7.18 (m, 2 H, Ar), 7.23 (t, ^3J = 7.6, 1 H, Ar), 7.31–7.35 (m, 3 H, Ar), 7.38 (d, ^3J = 7.9, 1 H, Ar), 7.86 (d, ^3J = 7.9, 1 H, Ar). ^{13}C-NMR (125.7 MHz, $CDCl_3$): δ_C = 13.9 (Me), 18.5 (CH_2), 21.8 (CH_2), 22.2 (CH_2), 33.1 (Me), 39.5 (CH_2), 126.1 (2 CH), 126.8 (C), 127.4 (2 CH), 127.8 (CH), 129.5 (C), 130.0 (CH), 130.7 (2 CH), 147.4 (C), 151.9 (C), 155.9 (C), 162.1 (C), 164.1 (C). MS: m/z (%) = 349 (M^+, 9), 292 (17), 258

(45), 244 (20), 91 (100), 57 (61). Anal. Calc. for $C_{21}H_{23}N_3S$ (349.49): C, 72.17; H, 6.63; N, 12.02%. Found: C, 72.19; H, 6.60; N, 12.06%.

***N*-(4-Fluorobenzyl)-3-pentylbenzo[*d*]imidazo[*5,1-b*]thiazol-1-amine (6k):** Cream powder; yield: 0.29 g (80%); mp: 127–130°C. IR (KBr) (ν_{max}, cm^{-1}): 3212, 1622, 1600, 1154. ^{1}H-NMR (500 MHz, $CDCl_3$): $\delta_H = 0.91$ (3 H, t, $^3J = 6.7$ Hz, Me), 1.19–1.22 (2 H, m, CH_2), 1.24–1.31 (4 H, m, CH_2), 2.01 (2 H, t, $^3J = 6.7$ Hz, CH_2), 2.99 (s, 2 H, CH_2), 6.01 (s, 1 H, NH), 7.41 (d, $^3J = 7.9$, 2 H, Ar), 7.58 (t, $^3J = 7.8$, 1 H, Ar), 7.70 (t, $^3J = 7.8$, 1 H, Ar), 7.72 (d, $^3J = 7.8$, 1 H, Ar),7.85 (d, $^3J = 7.8$, 1 H, Ar), 7.99 (d, $^3J = 7.9$, 2 H, Ar). ^{13}C-NMR (125.7 MHz, $CDCl_3$): $\delta_C = 13.7$ (Me), 20.7 (CH_2), 21.9 (CH_2), 22.0 (CH_2), 22.2 (CH_2), 38.0 (CH_2), 127.3 (2 CH), 129.8 (CH), 130.1 (2 CH), 131.2 (CH), 131.5 (CH), 132.0 (C), 133.0 (C), 135.6 (CH), 144.7 (C), 152.2 (C), 154.8 (C), 160.2 (C), 163.8 (C). MS: m/z (%) = 367 (M^+, 9), 296 (17), 272 (45), 258 (20), 106 (25), 95 (100), 71 (61). Anal. Calc. for $C_{21}H_{22}FN_3S$ (367.48): C, 68.64; H, 6.03; N, 11.43%. Found: C, 68.61; H, 6.00; N, 11.47%.

***N*-(4-Methylbenzyl)-3-pentylbenzo[*d*]imidazo[*5,1-b*]thiazol-1-amine (6l):** Cream powder; yield: 0.30 g (83%); mp: 119–121°C. IR (KBr) (ν_{max}, cm^{-1}): 3262, 1641, 1567, 1124. ^{1}H-NMR (500 MHz, $CDCl_3$): $\delta_H = 0.97$ (3 H, t, $^3J = 6.7$ Hz, Me), 1.24–1.27 (4 H, m, CH_2), 1.53–1.56 (2 H, m, CH_2), 2.13 (2 H, t, $^3J = 6.7$ Hz, CH_2), 2.15 (s, 3 H, Me), 2.47 (s, 2 H, CH_2), 4.90 (s, 1 H, NH), 7.16–7.23 (m, 3 H, Ar), 7.30–7.36 (m, 3 H, Ar), 7.40 (d, $^3J = 7.9$, 1 H, Ar), 7.90 (d, $^3J = 7.8$, 1 H, Ar). ^{13}C-NMR (125.7 MHz, $CDCl_3$): $\delta_C = 13.8$ (Me), 20.8 (CH_2), 22.2 (CH_2), 22.3 (CH_2), 30.7 (CH_2), 33.0 (Me), 126.2 (2 CH), 127.4 (2 CH), 130.2 (CH), 130.5 (CH), 130.7 (CH), 130.9 (C), 132.0 (CH), 142.1 (C), 146.8 (C), 146.9 (C), 149.7 (C), 149.8 (C), 160.7 (C), 164.3 (C).MS: m/z (%) = 363 (M^+, 9), 292 (17), 272 (45), 258 (20), 120 (25), 91 (100), 71 (61). Anal. Calc. for $C_{22}H_{25}N_3S$ (363.52): C, 72.69; H, 6.93; N, 11.56%. Found: C, 72.63; H, 6.90; N, 11.52%.

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