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Microwave-assisted synthesis of novel *N*-(4-phenylthiazol-2-yl)-benzo[*d*]thiazole-, thiazolo[4,5-*b*]pyridine-, thiazolo[5,4-*b*]pyridine- and benzo[*d*]oxazole-2-carboximidamides inspired by marine topsentines and nortopsentines

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ABSTRACT

We report the synthesis of novel *N*-(4-phenylthiazol-2-yl)-substituted benzo[*d*]thiazole-, thiazolo[4,5-*b*]pyridine-, thiazolo[5,4-*b*]pyridine- and benzo[*d*]oxazole-2-carboximidamides, which were inspired by marine topsentines and nortopsentines. Condensation of 4,5-dichloro-1,2,3-dithiazolium chloride (Appel salt) with various ortho-halogenated anilines, aminopyridines and aminophenols gave the corresponding aryliminodithiazoles in good to excellent yields. Copper(I)-mediated or nucleophilic-assisted cyclization of aryliminodithiazoles furnished cyano-functionalized benzo[*d*]thiazoles, thiazolo[4,5-*b*]- and thiazolo[5,4-*b*]-pyridines and benzo[*d*]oxazoles. The latter were condensed with substituted 4-phenylthiazol-2-amines to furnish twenty seven new polyaromatic carboximidamides in moderate to good yields.

1. Introduction

The occurrence and properties of the thiazolic ring in various natural and synthetic products has been the interest of many research groups on account of its useful biological properties.[1]

Ten years ago our laboratory launched a research program dealing with the preparation and pharmacological evaluation of original heterocyclic derivatives bearing a thiazole ring.[2]

In this context, the reactivity of 4,5-dichloro-1,2,3-dithiazolium chloride (Appel salt)[3] has been extensively studied for the synthesis of nitrile-bearing benzothiazoles with applications in the synthesis of functionalized heterocyclic systems.[4] To broaden the scope of our investigations on the synthesis of new molecules able to modulate the activity of kinases in signal transduction, we decided to explore the syntheses of benzo[*d*]thiazole-, thiazolo[4,5-*b*]pyridine-, thiazolo[5,4-*b*]pyridine-, benzo[*d*]oxazole-2-carbonitriles and their reactivity towards aromatic amines to access original hetero-aromatic carboximidamides (Fig. 1). The design of these novel tris-aromatic structures was largely inspired by topsentines and nortopsentines, two bisindoles alkaloids found in several marine sponges, which have received attention of various research groups because of their potent biological activities.[5]

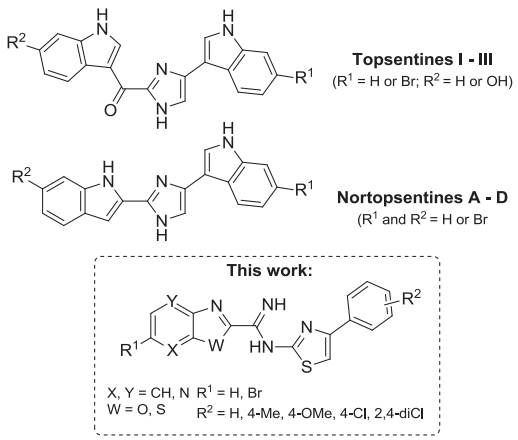

Fig. 1. Structures of marine alkaloids topsentines and nortopsentines, which inspired the current work on the synthesis of novel benzo[*d*]thiazole-, thiazolo[4,5-*b*]pyridine-, thiazolo[5,4-*b*]pyridine- and benzo[*d*]oxazole-2-carboximidamides.

This paper relates the development of a reliable synthetic route allowing access to novel benzo[*d*]thiazole-, thiazolo[4,5-*b*]

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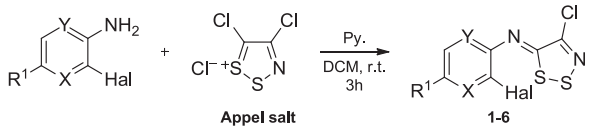
pyridine-, thiazolo[5,4-*b*]pyridine- and benzo[*d*]-oxazole-2-carboximidamides. Most of the chemistry performed in this study was achieved under microwave irradiation as a continuation of our global strategy, which consists of developing reactants and techniques offering operational, economic and environmental benefits over conventional methods.[6]

2. Results/discussion

In order to synthesize the desired carboximidamides, we considered the synthesis from simple commercially available compounds. The general retrosynthetic route depicted in Scheme 1 is based on previous work on the synthesis of carbonitrile-bearing benzo[*d*]thiazoles[3b] and benzo[*d*]oxazoles[2b] and was extended to novel thiazolo[4,5-*b*]pyridines and thiazolo[5,4- *b*]pyridines. Heterocyclic carboximidamides (**I**) would be obtained by the final condensation of substituted benzo[*d*]thiazole-, thiazolo[4,5-*b*]pyridine-, thiazolo[5,4-*b*]pyridine-, or benzo[*d*]oxazole-2-carbonitriles (**II**) on substituted 4-phenylthiazol-2-amines (**III**). 4-Phenylthiazol-2-amines would be synthesized by Hantzsch condensation of thiourea and substituted α-brominated acetophenones (**IV**). Thiazolo- and oxazolo-2-carbonitriles would be isolated after copper(I)-mediated cyclisation of ortho-halogenated *N*-aryliminodithiazoles and nucleophilic cyclization of ortho-hydroxylated *N*-arylimino-1,2,3-dithiazoles (**V**), respectively. Condensation of 4,5-dichloro-1,2,3-dithiazolium chloride (Appel salt) with various ortho-substituted anilines and aminopyridines (**VI**) would provide access to the desired *N*-aryliminodithiazoles.

Table 1
Synthesis of ortho-halogenated *N*-aryliminodithiazoles **1**–**6**

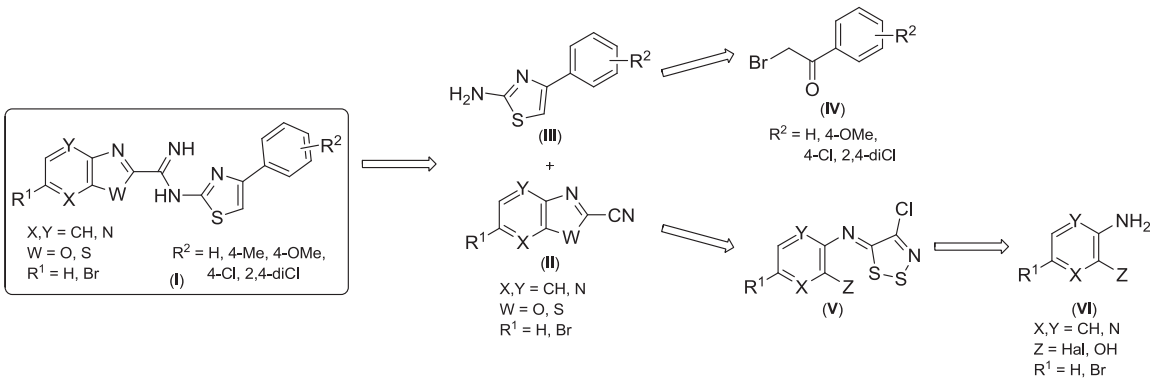


Entry	Product	Hal	X	Y	R^1	Yield (%)[a]
1	**1**	Br	CH	CH	H	97
2	**2**	Cl	CH	CH	H	98
3	**3**	Br	CH	CH	Br	96
4	**4**	Cl	N	CH	H	85
5	**5**	Br	N	CH	H	87
6	**6**	Br	CH	N	H	45

[a] Isolated yield.

Once the ortho-halogenated *N*-aryliminodithiazoles were isolated, they were converted and cyclized into benzothiazoles and thiazolopyridines in copper-catalyzed conditions.[7] Microwave-assisted irradiation of ortho-halogenated aryliminodithiazoles in the presence of copper(I) iodide in refluxing pyridine provided substituted benzo[*d*]thiazole-, thiazolo [4,5-*b*]-pyridine, thiazolo [5,4-*b*] pyridine-2-carbonitriles **7**–**9** in moderate to good yields (Table 2).

Table 2 highlights several important results regarding this copper(I)-mediated cyclization. Comparison of the results establishes that the use of ortho-brominated *N*-aryliminodithiazoles



Scheme 1. General retrosynthetic pathway and access to novel *N*-(4-phenylthiazol-2-yl)-substituted benzo[*d*]thiazole-, thiazolo[4,5-*b*]pyridine-, thiazolo[5,4-*b*]pyridine-, benzo[*d*]oxazole-2-carboximidamides.

Appel salt was readily synthesized from chloroacetonitrile and sulfur monochloride in multigram scale and stored on the bench away from light for months without apparent degradation.[3] In order to synthesize benzo[*d*]thiazole-, thiazolo[4,5-*b*]pyridine- and thiazolo[5,4-*b*]pyridine-2-carbonitriles, we initially carried out the synthesis of the corresponding ortho-halogenated *N*-aryliminodithiazoles **1**–**6**.

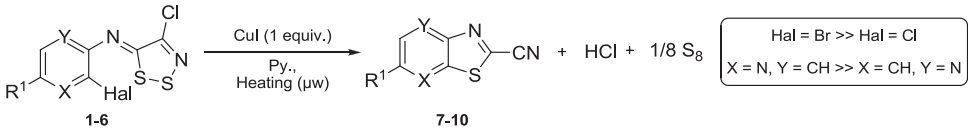
Condensation of electrophilic Appel salt with various ortho-haloanilines and aminopyridines in methylene chloride at room temperature followed by addition of pyridine gave the expected *N*-arylimino-1,2,3-dithiazoles **1**–**6** in good yields (Table 1).

Under the same operating conditions, most aryliminodithiazoles are obtained in good to excellent yields except in the case of compound **6**. In this last case, the relative position of the aromatic nitrogen atom and the deactivated amine function lead to a decreased nucleophilicity of 3-bromopyridin-2-amine thus preventing an effective condensation with Appel salt. On the other hand, the choice of the halogen atom does not have any influence on the condensation.

(Entries 1, 2, 4 and 5) had a beneficial effect on the copper(I)-mediated cyclisation compared to ortho-chlorinated *N*-arylimino-dithiazoles. Depending on the position the halogen atom, the pyridine moiety had a significant effect on the copper(I)-mediated cyclization. Indeed, the nitrogen atom had a favourable effect on the cyclization when the halogen atom is located at position C2 (Entries 4 and 5), indicating that the electron-deficient carbon–halogen bond assisted the cyclization process. However, the nitrogen atom had a deleterious effect on the cyclization when the halogen atom is positioned at C3 (Entry 6 and 7) suggesting that the electron-enriched carbon–halogen bond disfavoured the cyclization of **6** into thiazolo[5,4-*b*]pyridine-2-carbonitrile **10**. In fact, the complete conversion of **6** into **10** could only be achieved by microwave irradiation in sealed vials at a higher temperature (Entry 7). Attempts to run the same reaction by microwave irradiation at atmospheric pressure significantly decreased the cyclization yield of **6** into **10** and unknown by-products were observed (Entry 6).

In order to increase chemodiversity of the final topsentines and nortopsentines analogues, benzo[*d*]oxazole-2-carbonitriles **13** and

Table 2
Detailed conditions and yields for microwave-assisted copper(I)-mediated cyclisation of ortho-halogenated *N*-aryliminodithiazoles **1**–**6** into benzo[*d*]thiazole-2-carbonitriles **7** and **8**, thiazolo[4,5-*b*]pyridine-2-carbonitrile **9** and thiazolo[5,4-*b*]pyridine-2-carbonitrile **10**



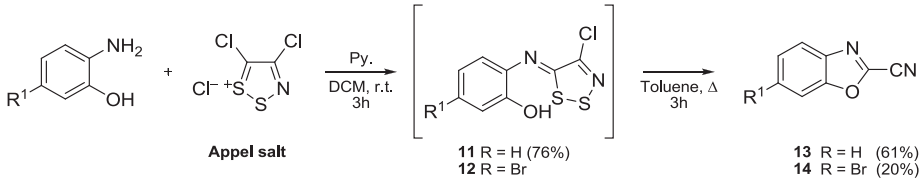
1-6 7-10

Entry	Starting material	Hal	X	Y	R^1	Conditions[a]	Product	X	Y	R^1	Yield (%)[b]
1	**1**	Br	CH	CH	H	115 °C, 30 min, CuI (1 equiv), py	**7**	CH	CH	H	43
2	**2**	Cl	CH	CH	H	115 °C, 30 min, CuI (1 equiv), py	**7**	CH	CH	H	—[c]
3	**3**	Br	CH	CH	Br	115 °C, 30 min, CuI (1 equiv), py	**8**	CH	CH	Br	63
4	**4**	Cl	N	CH	H	115 °C, 30 min, CuI (1 equiv), py	**9**	N	CH	H	31[d]
5	**5**	Br	N	CH	H	115 °C, 30 min, CuI (1 equiv), py	**9**	N	CH	H	72
6	**6**	Br	CH	N	H	115 °C, 6 h, CuI (2–4 equiv), py[e]	**10**	CH	N	H	25–30
7	**6**	Br	CH	N	H	130 °C, 1h, CuI (1 equiv), py	**10**	CH	N	H	45

[a] Entry 1–5 and 6: reactions were conducted in a microwave oven at atmospheric pressure (RotoSYNTH™). Entry 7: reaction was conducted in a microwave oven in a sealed tube (Anton Paar Monowave 300™). For details on experimental conditions, see Experimental section/Supplementary data.
[b] Isolated yield.
[c] Degradation of starting material.
[d] The major by-product of this reaction was the 2-chloro-3-isothiocyanatopyridine derived from **4**.
[e] In the first trial, another equiv of CuI was added after 3 h of heating; the second experiment was started with 2 equiv of CuI, and 2 equiv were also added after 3 h of irradiation.

14 were synthesized starting from aminophenols with modest 20–61% overall yields (Scheme 2). Condensation of Appel salt with aminophenols under the same conditions as those described above provided thermosensitive ortho-hydroxylated aryliminodithiazoles **11** (76% yield) and **12** (not isolated), which quickly cyclized in refluxing toluene into benzo[*d*]oxazole-2-carbonitriles **13**[8] and **14**, upon loss of sulfur and hydrogen chloride (Scheme 2).

Different strategies were implemented to effectively perform the condensation of the newly synthesized heteroaromatic carbonitriles **7**–**10** with substituted 4-phenylthiazole-2-amines **15**–**18**: activation of the carbonitrile function ($AlCl_3$, THF, microwave), activation of the amine function (NaH, DMF, then addition of carbonitrile), or direct microwave-assisted high-temperature condensation. Among these three methods, the last one gave the best



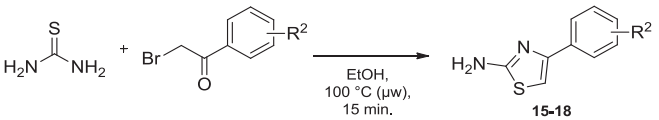
Scheme 2. Synthesis of benzo[*d*]oxazole-2-carbonitriles **13**–**14** using 4,5-dichloro-1,2,3-dithiazolium chloride and aminophenols.

The reactivity of aromatic carbonitriles **7**–**10** and **13**–**14** was tested against aromatic substituted 4-phenylthiazol-2-amines **15**–**18** in order to get a new set of carboximidamides **19**–**45** with a potential biological activity. In addition to our wish to find novel inhibitors of kinases that include thiazole, it may be noted that recent studies have shown the importance of tris-aromatic structures with a thiazole moiety in various biological activities, including antibacterial, antimicrobial, anti-oxidant, anti-fungal and antiproliferative.[9]

The lack of structure–activity relationship features among the studied 4-phenyl-thiazol-2-amines **15**–**18** prompted us to employ the Topliss scheme for selecting the substitution patterns on the aromatic substituent of these heterocyclic amines.[11] In the case of our study, four substituted α-bromoacetophenones were chosen according to Topliss diagram (Table 3) so as to check the interest of our methodology, while starting building a short list of molecules with potential biological interest. Although there were only few commercially available compounds, the synthesis of these heteroaromatic amines proved to be very straightforward thanks to an optimization under microwave. Irradiating a mixture of thiourea and substituted α-bromoacetophenone, in ethanol for 15 min provided 4-phenylthiazole-2-amines **15**–**18** in excellent yields (Table 3).

results: microwave irradiation of the carbonitrile and the amine under pressure in DMF for at least 3 h at 180 °C gave the desired substituted *N*-(4-phenylthiazol-2-yl)-benzo[*d*]thiazole-2-carboximidamides (**19**–**28**), thiazolo[4,5-*b*]pyridines (**29**–**33**), thiazolo[5,4-*b*]pyridine- (**34**–**35**), benzo[*d*]oxazole-2-carboximidamides (**36**–**45**) in moderate to satisfactory yields (Table 4).

Table 3
Yields for the microwave-assisted synthesis of substituted 4-phenylthiazol-2-amines **15**–**18** using thiourea and α-brominated acetophenones[10]



15-18

Product	R^2	Yield (%)[a]
15	H	90
16	4-OMe	91
17	4-Cl	91
18	2,4-diCl	89

[a] Isolated yield.

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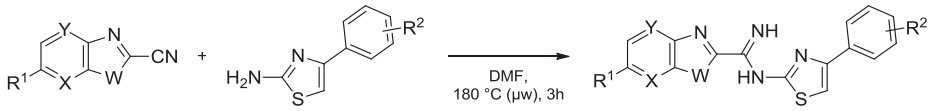
Table 4
Detailed conditions and yields for the microwave-assisted synthesis of novel substituted *N*-(4-phenylthiazol-2-yl)-benzo[*d*]thiazole-, thiazolo[4,5-*b*]pyridine-, thiazolo[5,4-*b*]pyridine-, benzo[*d*]oxazole-2-carboximidamides **19**–**45**[a]



7-10, 13, 14 15-18 19-45

Starting material[a]	W	X	Y	R^1	R^2	Product	Yield (%)[b]
7	S	CH	CH	H	H	**19**	80
7	S	CH	CH	H	4-Me	**20**	72
7	S	CH	CH	H	4-OMe	**21**	44
7	S	CH	CH	H	4-Cl	**22**	40
7	S	CH	CH	H	2,4-diCl	**23**	50
8	S	CH	CH	Br	H	**24**	73
8	S	CH	CH	Br	4-Me	**25**	74
8	S	CH	CH	Br	4-OMe	**26**	82
8	S	CH	CH	Br	4-Cl	**27**	65
8	S	CH	CH	Br	2,4-diCl	**28**	33
9	S	N	CH	H	H	**29**	56
9	S	N	CH	H	4-Me	**30**	39
9	S	N	CH	H	4-OMe	**31**	63
9	S	N	CH	H	4-Cl	**32**	38
9	S	N	CH	H	2,4-diCl	**33**	47
10	S	CH	N	H	4-Me	**34**	58
10	S	CH	N	H	4-OMe	**35**	77
13	O	CH	CH	H	H	**36**	56
13	O	CH	CH	H	4-Me	**37**	39
13	O	CH	CH	H	4-OMe	**38**	63
13	O	CH	CH	H	4-Cl	**39**	38
13	O	CH	CH	H	2,4-diCl	**40**	47
14	O	CH	CH	Br	H	**41**	56
14	O	CH	CH	Br	4-Me	**42**	51
14	O	CH	CH	Br	4-OMe	**43**	52
14	O	CH	CH	Br	4-Cl	**44**	44
14	O	CH	CH	Br	2,4-diCl	**45**	42

[a] All reactions were conducted in a microwave oven in a sealed tube (Anton Paar Monowave 300™). For details on experimental conditions, see Experimental section/Supplementary data.
[b] Isolated yield.

Biological experiments were performed in order to evaluate the capacity of the tris-aromatic compounds **19**–**45** to inhibit a panel of Ser/Thr and Tyr kinases, which are considered as relevant therapeutic targets.[12] Unfortunately, whatever the kinase tested, none of the twenty-seven tested molecules showed a significant effect on enzymes activity.

Some comments can be made concerning the microwave procedure as well as the technical and practical aspects. In the case of the microwave-assisted synthesis, DMF and pyridine offer the advantage of having good dielectric properties, thus enabling an efficient heating of the reaction mixture.[13] Copper(I)-mediated cyclizations were carried out at atmospheric pressure on a RotoSYNTH™ (Milestone S.r.l. Italy), a multimode cavity, with temperature and power control (except in the case of **10**). Carboximidamides syntheses were performed in sealed vials in a Monowave 300™ single-mode reactor (Anton Paar GmbH, Graz, Austria) under temperature control mode and not in constant power mode. Temperature was monitored via contactless-infrared pyrometer, which was calibrated by control experiments with a fiber-optic thermometer (Ruby thermometer).

3. Conclusion

In conclusion, this synthetic work allowed the preparation of a large range of valuable functionalized heterocyclic scaffolds in a straightforward and sustainable manner. Thus, the efficient microwave-assisted synthesis of novel substituted *N*-(4-phenylthiazol-2-yl)benzo[*d*]thiazole- (**19**–**28**), thiazolo[4,5-*b*]pyridine- (**29**–**33**), thiazolo[5,4-*b*]pyridine- (**34**, **35**) and benzo[*d*]oxazole-2-carboximidamide derivatives (**36**–**45**) was described. Appel salt proved to be an effective reagent for the synthesis of various benzo[*d*]thiazole-, thiazolo[4,5- or 5,4-*b*]pyridine- and benzo[*d*]oxazole-2-carbonitriles. A study established that the relative position of the nitrogen and the nature of the halogen atom of ortho-halogenated aryliminodithiazoles (e.g., **1**–**6**) had an important influence on the performance of the copper(I)-assisted cyclization.

Although Ser/Thr and Tyr kinases have not shown a relevant affinity for these novel compounds, work is underway to screen the carboximamides on new biological targets in order to conceive new useful heterocycles with potential therapeutic applications.

4. Experimental section

4.1. General methods

All reactions were carried out under inert atmosphere of argon or nitrogen and monitored by thin-layer chromatography with silica gel 60 F_{254} pre-coated aluminium plates (0.25 mm). Visualization was performed with a UV light at 254 and 312 nm.

Purifications were carried out on an Armen Instrument Spot 2 Flash System equipped with a dual UV–vis spectrophotometer (200–600 nm), a fraction collector (192 tubes), a dual piston pump (1–250 mL/min, P_{max}=35 bar/508 psi) allowing quaternary gradients and an additional inlet for air purge. Samples can be injected in liquid or solid mode. Purification was edited and monitored on an integrated panel PC with a touch screen controlled by Armen Glider

Flash v3.1d software. Biotage SNAP flash chromatography cartridges (KP-Sil, normal phase, 10–340 g) were used for the purification process.

Melting points of solid compounds were measured on a Stuart™ melting point apparatus SMP3 and are uncorrected. IR spectra were recorded on a PerkinElmer Spectrum 100 Series FT-IR spectrometer. Liquids and solids were applied on the Single Reflection Attenuated Total Reflectance (ATR) Accessories. Absorption bands are given in cm^{-1}.

^{1}H, ^{13}C NMR spectra were recorded on a Bruker DXP 300 spectrometer at 300 and 75 MHz, respectively. Abbreviations used for peak multiplicities are s: singlet, br s: broad singlet, d: doublet, t: triplet, q: quadruplet and m: multiplet. Coupling constants *J* are in Hertz and chemical shifts are given in parts per million and calibrated with DMSO-d_6 (residual solvent signals). Mass spectra analysis was performed by the Mass Spectrometry Laboratory of the University of Rouen. Mass spectra (EI) were recorded with a Waters LCP 1er XR spectrometer.

Microwave experiments were conducted in two different commercial microwave reactors especially designed for synthetic chemistry. Time indicated in the various protocols is the time measured when the mixtures reached the programmed temperature after a ramp period of 2 min.

- RotoSYNTH (Milestone S.r.l. Italy) is a multimode cavity with a microwave power delivery system ranging from 0 to 1200 W. Open vessel experiments (atmospheric pressure) were carried out in round bottom flask (from 25 mL to 4 L) fitted with a reflux condenser. The temperature was monitored via a contact-less infrared pyrometer (IRT) and fiber-optic contact thermometer (FO). Temperature, pressure and power profiles were edited and monitored through the EASY-Control software provided by the manufacturer.
- Anton Paar Monowave 300 is a monomode cavity with a microwave power delivery system ranging from 0 to 850 W allowing pressurized reactions (0–30 bars) to be carried out in sealed glass vials (4–30 mL) equipped a snap cap and a silicon septum. The temperature (0–300 °C) was monitored via a contact-less infrared sensor and a Ruby Thermometer. Temperature, pressure and power profiles were edited and monitored through a touch screen control panel.

4.2. Synthesis of ortho-halogenated *N*-aryliminodithiazoles using 4,5-dichloro-1,2,3-dithiazolium chloride (Appel salt)

4,5-Dichloro-1,2,3-dithiazolium chloride (5.421 g, 26 mmol) was added portionwise to a stirred solution of the appropriate amine (20 mmol) in freshly distilled methylene chloride (150 mL) at room temperature. The dark mixture was vigorously agitated for 3 h. Pyridine (40 mmol, 3.23 mL) was added dropwise to the solution, which was further agitated for another 2 h. The reaction mixture was quenched with water. The organic layer was separated and dried over magnesium sulfate and evaporated to dryness in vacuo. Purification of the dark brown residue by flash chromatography using petroleum ether/methylene chloride (100:0 to 0:100, v/v) as eluent afforded the corresponding aryliminodithiazoles.

*4.2.1. (Z)-2-Bromo-N-(4-chloro-5H-1,2,3-dithiazol-5-ylidene) aniline (**1**).* Yield 97% (5.968 g), yellow solid, mp=80–82 °C; IR (cm^{-1}) υ_{max} 3065, 1691, 1661, 1596, 1583, 1540, 1503, 1463, 1433, 1223, 1150, 1042, 1024, 856, 848, 771, 720, 673; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.76 (dd, *J*=8.0, 0.9 Hz, 1H, *H*-3), 7.55–7.43 (m, 1H, H_{ar}), 7.27–7.13 (m, 2H, H_{ar}); ^{13}C NMR (75 MHz, DMSO-d_6) δ 163.0, 150.9, 146.8, 134.1, 130.1, 127.7, 119.2, 114.8; HRMS calcd for $C_8H_5^{79}BrClN_2S_2$ $[M+H]^+$ 306.8771, found 306.8766.

*4.2.2. (Z)-2,4-Dibromo-N-(4-chloro-5H-1,2,3-dithiazol-5-ylidene) aniline (**3**).* Yield 96% (7.421 g), yellow solid, mp=120–122 °C; IR (cm^{-1}) υ_{max} 3080, 2963, 1591, 1543, 1513, 1458, 1376, 1257, 1232, 1154, 1130, 1080, 1041, 861, 851, 810, 795, 776, 712, 649, 533; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.01 (d, *J*=2.1 Hz, 1H, *H*-3), 7.68 (dd, *J*=8.5, 2.1 Hz, 1H, *H*-5), 7.22 (d, *J*=8.5 Hz, 1H, *H*-6); ^{13}C NMR (75 MHz, DMSO-d_6) δ 163.6, 150.2, 146.7, 136.0, 133.1, 121.1, 118.5, 116.1; HRMS calcd for $C_8H_4^{79}Br_2ClN_2S_2$ $[M+H]^+$ 384.7871, found 384.7876.

*4.2.3. (Z)-2-Chloro-N-(4-chloro-5H-1,2,3-dithiazol-5-ylidene) pyridin-3-amine (**4**).* Yield 85% (4.490 g), yellow solid, mp=144–146 °C; IR (cm^{-1}) υ_{max} 3050, 1581, 1565, 1554, 1505, 1442, 1397, 1206, 1155, 1082, 1065, 869, 795, 779, 742, 707, 662; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.29 (d, *J*=4.0 Hz, 1H, *H*-6), 7.76 (d, *J*=7.6 Hz, 1H, *H*-4), 7.55 (dd, *J*=7.6, 4.0 Hz, 1H, *H*-5); ^{13}C NMR (75 MHz, DMSO-d_6) δ 164.8, 147.0, 146.7, 145.7, 142.0, 128.8, 125.2; HRMS calcd for $C_7H_4Cl_2N_3S_2$ $[M+H]^+$ 263.9224, found 263.9226.

*4.2.4. (Z)-2-Bromo-N-(4-chloro-5H-1,2,3-dithiazol-5-ylidene) pyridin-3-amine (**5**).* Yield 87% (5.335 g), brown solid, mp=144–146 °C; IR (cm^{-1}) υ_{max} 3361, 3037, 1585, 1391, 1154, 1068, 1057, 867, 794, 776, 734, 694, 654, 610; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.25 (dd, *J*=4.6, 1.7 Hz, 1H, *H*-6), 7.70 (dd, *J*=7.9, 1.7 Hz, 1H, *H*-4), 7.56 (dd, *J*=7.9, 4.6 Hz, 1H, *H*-5); ^{13}C NMR (75 MHz, DMSO-d_6) δ 164.8, 147.7, 147.4, 146.7, 134.9, 128.1, 125.4; HRMS calcd for $C_7H_4^{79}BrClN_3S_2$ $[M+H]^+$ 307.8719, found 307.8716.

*4.2.5. (Z)-3-Bromo-N-(4-chloro-5H-1,2,3-dithiazol-5-ylidene) pyridin-2-amine (**6**).* Yield 45% (2.777 g), yellow solid, mp=180–182 °C; IR (cm^{-1}) υ_{max} 3072, 1573, 1551, 1514, 1483, 1413, 1277, 1229, 1170, 1032, 895, 869, 787, 625; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.69 (dd, *J*=4.8, 1.3 Hz, 1H, *H*-6), 8.36 (dd, *J*=7.8, 1.3 Hz, 1H, *H*-4), 7.37 (dd, *J*=7.8, 4.8 Hz, 1H, *H*-5); ^{13}C NMR (75 MHz, DMSO-d_6) δ 160.6, 152.5, 149.2, 144.1, 143.2, 123.7, 118.3; HRMS calcd for $C_7H_4^{79}BrClN_3S_2$ $[M+H]^+$ 307.8719, found 307.8716.

4.3. Microwave-assisted copper(I)-mediated cyclization of ortho-bromoaryliminodithiazoles (7–10)

A stirred solution of the appropriate aryliminodithiazole (15 mmol) and copper iodide (CuI, 2.857 g, 15 mmol) in dry pyridine (150 mL) was heated under microwave irradiation (400 W) at 115 °C for 30 min at atmospheric pressure. The dark solution was evaporated in vacuo. The resulting black residue was dissolved in ethyl acetate and washed with a saturated solution of sodium thiosulfate and brine. The organic layer was dried over magnesium sulfate and evaporated in vacuo. Purification of the dark brown residue by flash chromatography using petroleum ether/methylene chloride (100:0 to 0:100, v/v) (benzothiazole series) or methylene chloride/ethyl acetate (100:0 to 0:100, v/v) (thiazolopyridine series) as eluent afforded the corresponding cyano derivatives.

*4.3.1. Benzo[d]thiazole-2-carbonitrile (**7**).* Yield 43% (1.032 g), colourless solid, mp=75–77 °C; IR (cm^{-1}) υ_{max} 3084, 3066, 2229, 1550, 1466, 1455, 1421, 1317, 1242, 1148, 1133, 1122, 874, 759, 726, 702; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.45–8.32 (m, 1H, H_{ar}), 8.31–8.22 (m, 1H, H_{ar}), 7.79–7.64 (m, 1H, H_{ar}); ^{13}C NMR (75 MHz, DMSO-d_6) δ152.2, 137.6, 135.9, 129.2, 128.6, 125.1, 123.6, 113.9; HRMS calcd for $C_8H_5N_2S$ $[M+H]^+$ 161.0173, found 161.0170.

*4.3.2. 6-Bromobenzo[d]thiazole-2-carbonitrile (**8**).* Yield 63% (2.259 g), colourless solid, mp=140–142 °C; IR (cm^{-1}) υ_{max} 3083,

2231, 1581, 1536, 1464, 1389, 1307, 1144, 1075, 861, 815; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.66 (d, J=1.9 Hz, 1H, H-7), 8.21 (d, J=8.8 Hz, 1H, H-4), 7.89 (dd, J=8.8, 2.0 Hz, 1H, H-5); ^{13}C NMR (75 MHz, DMSO-d_6) δ 151.2, 138.7, 137.9, 132.0, 126.5, 126.2, 122.4, 113.6; HRMS calcd for $C_8H_3^{79}BrN_2S$ $[M-H]^-$ 238.9279, found 237.9192.

*4.3.3. Thiazolo[5,4-b]pyridine-2-carbonitrile (**9**).* Yield 72% (1.741 g), colourless solid, mp=136–138 °C (lit.,[14] 135 °C); IR (cm^{-1}) υ_{max} 2925, 2232, 1573, 1551, 1461, 1438, 1374, 1277, 1246, 1166, 1153, 1114, 806, 747, 703, 630; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.91 (dd, J=4.6, 1.2 Hz, 1H, H-6), 8.72 (dd, J=8.4, 1.2 Hz, 1H, H-4), 7.82 (dd, J=8.4, 4.6 Hz, 1H, H-5); ^{13}C NMR (75 MHz, DMSO-d_6) δ 157.8, 152.1, 145.2, 138.0, 133.4, 124.1, 113.5; HRMS calcd for $C_7H_4N_3S$ $[M+H]^+$ 162.0126, found 162.0129.

*4.3.4. Thiazolo[4,5-b]pyridine-2-carbonitrile (**10**).* Yield 45% (0.991 g), colourless solid, mp=140–142 °C; IR (cm^{-1}) υ_{max} 3072, 2923, 2236, 1538, 1469, 1377, 1306, 1291, 1137, 808, 772, 728, 714; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.95 (dd, J=4.4, 1.3 Hz, 1H, H-5), 8.85 (dd, J=8.3, 1.3 Hz, 1H, H-7), 7.73 (dd, J=8.3, 4.4 Hz, 1H, H-6); ^{13}C NMR (75 MHz, DMSO-d_6) δ 160.2, 149.4, 139.7, 131.8, 128.2, 121.4, 111.7; HRMS calcd for $C_7H_4N_3S$ $[M+H]^+$ 162.0126, found 162.0130.

4.4. Synthesis of benzo[*d*]oxazole-2-carbonitriles (13 and 14)

4,5-Dichloro-1,2,3-dithiazolium chloride (4.066 g, 19.5 mmol) was added portionwise to a stirred solution of the appropriate aminophenol (15 mmol) in freshly distilled methylene chloride (115 mL) at room temperature. The dark mixture was vigorously agitated for 3 h. Pyridine (30 mmol, 2.42 mL) was added dropwise to the solution, which was further agitated for another 2 h. The reaction mixture was quenched with water. The organic layer was separated and dried over magnesium sulfate and evaporated to dryness in vacuo. (*Z*)-2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)phenol was purified by flash chromatography using petroleum ether/methylene chloride (100:0 to 0:100, v/v) or directly engaged in the cyclization step.

(*Z*)-2-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)phenol was dissolved in toluene (50 mL) and vigorously refluxed for 3 h. The reaction mixture was evaporated in vacuo. Purification of the residue by flash chromatography using petroleum ether/methylene chloride (100:0 to 0:100, v/v) afforded the corresponding benzo[*d*]oxazole-2-carbonitriles.

*4.4.1. (Z)-2-(4-Chloro-5H-1,2,3-dithiazol-5-ylideneamino)phenol (**11**).* Yield 76% (3.71 g), yellow solid, mp=183–185 °C; IR (cm^{-1}) υ_{max} 3385, 1661, 1608, 1583, 1472, 1444, 1339, 1286, 1254, 1219, 1135, 1033, 951, 854, 807, 744, 730, 674; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.46 (br s, 1H, O*H*), 7.12–7.03 (m, 1H, H_{ar}), 7.02–6.94 (m, 2H, H_{ar}), 6.87 (td, J=7.8, 1.4 Hz, 1H, H_{ar}); ^{13}C NMR (75 MHz, DMSO-d_6) δ 160.7, 148.0, 147.2, 139.4, 127.4, 120.3, 119.8, 117.3; HRMS calcd for $C_8H_5N_2O$ $[M+H]^+$ 244.9610, found 244.9607.

*4.4.2. Benzo[d]oxazole-2-carbonitrile (**13**).* Yield 61% (1.317 g), colourless solid, mp=102–104 °C; IR (cm^{-1}) υ_{max} 2249, 1530, 1475, 1443, 1338, 1256, 1169, 1102, 950, 893, 817, 759, 748, 685, 620; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.00 (d, J=8.0 Hz, 1H, H_{ar}), 7.94 (d, J=8.3 Hz, 1H, H_{ar}), 7.74–7.67 (m, 1H, H_{ar}), 7.63–7.56 (m, 1H, H_{ar}); ^{13}C NMR (75 MHz, DMSO-d_6) δ 150.6, 139.4, 137.8, 129.9, 127.2, 122.0, 112.4, 110.2. This compound was already described[2b,5], spectrometric data are consistent with the assigned structure.

*4.4.3. 6-Bromobenzo[d]oxazole-2-carbonitrile (**14**).* Yield 20% (0.665 g), light brown solid, mp=148–150 °C; IR (cm^{-1}) υ_{max} 3086, 2249, 1599, 1528, 1412, 1324, 1257, 1190, 954, 908, 857, 820, 689, 594; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.31 (d, J=1.8 Hz, 1H, H-7), 7.93 (d, J=8.6 Hz, 1H, H-4), 7.75 (dd, J=8.6, 1.8 Hz, 1H, H-5); ^{13}C NMR (75 MHz, DMSO-d_6) δ 151.0, 138.8, 138.3, 130.6, 123.4, 122.3, 115.8, 109.9; HRMS calcd for $C_8H_4^{79}BrN_2O$ $[M+H]^+$ 222.9507, found 222.9505.

4.5. Microwave-assisted synthesis of substituted 4-phenylthiazol-2-amines (15–18) via Hantzsch condensation

In a sealed tube, a stirred solution of thiourea (10.91 mmol) and the appropriate α-bromoacetophenone (10.91 mmol) in ethanol (15 mL) was irradiated (800 W) at 100 °C for 15 min. The solvent was evaporated to dryness. The solid residue was neutralized with a saturated solution of sodium bicarbonate and extracted three times with methylene chloride. The organic layer was dried over magnesium sulfate and the solvent was evaporated to dryness. The solid residue was agitated for 30 min in cyclohexane and filtered off to afford the 4-phenylthiazol-2-amine in analytically pure form.

*4.5.1. 4-Phenylthiazol-2-amine (**15**).* Yield 90% (1.730 g), colourless solid, mp=151–153 °C (lit.,[15] 151 °C); IR (cm^{-1}) υ_{max} 3432, 3246, 3156, 3111, 1595, 1515, 1482, 1329, 1037, 909, 845, 772, 712, 665; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.79 (d, J=7.5 Hz, 2H), 7.36 (t, J=7.5 Hz, 2H), 7.25 (t, J=7.2 Hz, 1H), 7.06 (br s, 2H, NH_2), 6.99 (s, 1H, $H_{thiazole}$); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.0, 150.6, 135.5, 129.0 (2C), 127.7, 126.1 (2C), 101.9; HRMS calcd for $C_9H_9N_2S$ $[M+H]^+$ 177.0486, found 177.0485.

*4.5.2. 4-(4-Methoxyphenyl)thiazol-2-amine (**16**).* Yield 91% (2.048 g), colourless solid, mp=208–210 °C (lit.,[15] 209 °C); IR (cm^{-1}) υ_{max} 3427, 3258, 3116, 1622, 1535, 1517, 1490, 1414, 1287, 1242, 1176, 1032, 833, 735, 696; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.72 (d, J=8.7 Hz, 2H, H-Ph), 7.00 (br s, 2H, NH_2), 6.92 (d, J=8.7 Hz, 2H, H-Ph), 6.82 (s, 1H, $H_{thiazole}$), 3.76 (s, 3H, Ph-OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.9, 159.3, 150.4, 128.4, 127.4 (2C), 114.3 (2C), 99.7, 55.2; HRMS calcd for $C_{10}H_{11}N_2OS$ $[M+H]^+$ 207.0592, found 207.0585.

*4.5.3. 4-(4-Chlorophenyl)thiazol-2-amine (**17**).* Yield 91% (2.091 g), colourless solid, mp=171–173 °C (lit.,[15] 168 °C); IR (cm^{-1}) υ_{max} 3435, 3271, 3089, 1631, 1531, 1474, 1399, 1329, 1085, 1035, 1008, 821, 728, 665; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.81 (d, J=8.5 Hz, 2H, H-Ph), 7.41 (d, J=8.5 Hz, 2H, H-Ph), 7.11 (br s, 2H, NH_2), 7.07 (s, 1H, $H_{thiazole}$); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.2, 149.3, 134.4, 132.1, 129.0 (2C), 127.8 (2C), 102.7; HRMS calcd for $C_9H_8ClN_2S$ $[M+H]^+$ 211.0097, found 211.0092.

*4.5.4. 4-(2,4-Dichlorophenyl)thiazol-2-amine (**18**).* Yield 89% (2.38 g), light brown solid, mp=166–168 °C (lit.,[15] 163 °C); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.87 (d, J=8.5 Hz, 1H, H-Ph), 7.64 (d, J=2.2 Hz, 1H, H-Ph), 7.45 (dd, J=8.5, 2.2 Hz, 1H, H-Ph), 7.11 (s, 3H, NH_2+$H_{thiazole}$); ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.2, 145.9, 133.0, 132.9, 132.7, 131.9, 130.3, 127.9, 107.5; IR (cm^{-1}) υ_{max} 3451, 3269, 3111, 1630, 1536, 1461, 1370, 1334, 1194, 1101, 1025, 834, 811, 784, 694; HRMS calcd for $C_9H_7Cl_2N_2S$ $[M+H]^+$ 244.9707, found 244.9704.

4.6. Microwave-assisted synthesis of *N*-(4-phenylthiazol-2-yl)-benzo[*d*]thiazole-, thiazolo[4,5-*b*]pyridine-, thiazolo[5,4-*b*]pyridine-, benzo[*d*]oxazole-2-carboximidamides (19–45)

In a sealed tube, a stirred solution of carbonitrile (2 mmol) and the appropriate 4-phenylthiazol-2-amine (2.4 mmol) in dry DMF (4 mL) was heated under microwave irradiation (800 W) at 180 °C for 3 h. Evaporation of the solvent gave a crude product, which was purified by flash chromatography using petroleum ether/methylene chloride (100:0 to 0:100, v/v) as eluent.

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*4.6.1. N-(4-Phenylthiazol-2-yl)benzo[d]thiazole-2-carboximidamide (**19**).* Yield 80% (0.536 g), yellow solid, mp=228–230 °C; IR (cm^{-1}) υ_{max} 3364, 3107, 2914, 1619, 1592, 1537, 1509, 1476, 1318, 1234, 1117, 1044, 818, 766, 754, 726, 619; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.54 (br s, bs, 1H, N*H*), 9.26 (br s, 1H, N*H*), 8.25–8.19 (m, 1H, H_{ar}), 8.16 (d, J=7.5 Hz, 1H, H_{ar}), 7.95 (d, J=7.2 Hz, 2H, *H*-Ph), 7.84 (s, 1H, $H_{thiazole}$), 7.68–7.55 (m, 2H, H_{ar}), 7.48 (t, J=7.5 Hz, 2H, *H*-Ph), 7.37 (t, J=7.3 Hz, 1H, *H*-Ph); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.2, 165.6, 153.7, 151.8, 151.7, 136.9, 134.6, 129.4 (2C), 128.7, 127.6, 127.5, 126.3 (2C), 124.2, 123.4, 110.6; HRMS calcd for $C_{17}H_{13}N_4S_2$ $[M+H]^+$ 337.0582, found 337.0596.

*4.6.2. N-(4-p-Tolylthiazol-2-yl)benzo[d]thiazole-2-carboximidamide (**20**).* Yield 72% (0.505 g), yellow solid, mp=199–201 °C; IR (cm^{-1}) υ_{max} 3364, 3107, 2914, 1619, 1592, 1537, 1509, 1476, 1451, 1318, 1234, 1214, 1117, 1044, 818, 754, 726, 619, 488; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.40 (br s, 2H, N*H*+N*H*), 8.22 (d, J=7.4 Hz, 1H, H_{ar}), 8.16 (d, J=7.4 Hz, 1H, H_{ar}), 7.84 (d, J=8.0 Hz, 2H, *H*-Ph), 7.75 (s, 1H, $H_{thiazole}$), 7.70–7.53 (m, 2H, H_{ar}), 7.29 (d, J=8.0 Hz, 2H, *H*-Ph), 2.35 (s, 3H, Ph-CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.1, 165.6, 153.7, 151.7, 151.6, 138.0, 136.8, 131.9, 129.9 (2C), 127.5, 127.4, 126.2 (2C), 124.2, 123.3, 109.7, 20.7; HRMS calcd for $C_{18}H_{15}N_4S_2$ $[M+H]^+$ 351.0738, found 351.0739.

*4.6.3. N-[4-(4-Methoxyphenyl)thiazol-2-yl]benzo[d]thiazole-2-carboximidamide (**21**).* Yield 44% (0.349 g), yellow solid, mp=249–251 °C; IR (cm^{-1}) υ_{max} 3457, 1609, 1598, 1519, 1481, 1301, 1252, 1030, 833, 734, 694, 631, 588, 454; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.46 (br s, 1H, N*H*), 9.27 (br s, 1H, N*H*), 8.24–8.13 (m, 2H, H_{ar}), 7.88 (d, J=8.8 Hz, 2H, *H*-Ph), 7.66 (s, 1H, $H_{thiazole}$), 7.65–7.55 (m, 2H, H_{ar}), 7.04 (d, J=8.8 Hz, 2H, H-Ph), 3.81 (s, 3H, Ph-OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.0, 165.6, 159.9, 153.7, 151.6, 151.5, 136.8, 127.7 (2C), 127.5, 127.4, 127.3, 124.2, 123.3, 114.7 (2C), 108.5, 55.3; HRMS calcd for $C_{18}H_{15}N_4OS_2$ $[M+H]^+$ 367.0687, found 367.0690.

*4.6.4. N-(4-(4-Chlorophenyl)thiazol-2-yl)benzo[d]thiazole-2-carboximidamide (**22**).* Yield 40% (0.297 g), yellow solid, mp=234–236 °C; IR (cm^{-1}) υ_{max} 3362, 3252, 3221, 1622, 1591, 1537, 1511, 1470, 1449, 1401, 1314, 1230, 1124, 1094, 1013, 867, 832, 754, 727, 609, 515; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.34 (br s, 2H, N*H*+N*H*), 8.24–8.14 (m, 2H, H_{ar}), 7.98 (d, J=8.6 Hz, 2H, *H*-Ph), 7.89 (s, 1H, $H_{thiazole}$), 7.67–7.56 (m, 2H, H_{ar}), 7.53 (d, J=8.6 Hz, 2H, *H*-Ph); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.3, 165.5, 153.7, 151.8, 150.5, 136.9, 133.4, 133.1, 129.4 (2C), 128.1 (2C), 127.6, 127.5, 124.2, 123.3, 111.3; HRMS calcd for $C_{17}H_{12}ClN_4S_2$ $[M+H]^+$ 371.0192, found 371.0188.

*4.6.5. N-(4-(2,4-Dichlorophenyl)thiazol-2-yl)benzo[d]thiazole-2-carboximidamide (**23**).* Yield 50% (0.405 g), yellow solid, mp=212–214 °C; IR (cm^{-1}) υ_{max} 3454, 3257, 3100, 3055, 1603, 1526, 1465, 1235, 1101, 1044, 858, 757; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.35 (br s, 2H, N*H*+N*H*), 8.24–8.13 (m, 2H, H_{ar}), 7.89 (d, J=8.4 Hz, 1H, *H*-Ph), 7.80 (s, 1H, $H_{thiazole}$), 7.76 (d, J=2.1 Hz, 1H, *H*-Ph), 7.68–7.53 (m, 3H, H_{ar}+*H*-Ph); ^{13}C NMR (75 MHz, DMSO-d_6) δ 172.5, 165.4, 153.7, 152.0, 147.4, 136.8, 133.8, 133.0, 132.5, 132.4, 130.5, 128.2, 127.5, 127.4, 124.2, 123.3, 115.7; HRMS calcd for $C_{17}H_{11}Cl_2N_4S_2$ $[M+H]^+$ 404.9802, found 404.9802.

*4.6.6. 6-Bromo-N-(4-phenylthiazol-2-yl)benzo[d]thiazole-2-carboximidamide (**24**).* Yield 73% (0.606 g), yellow solid, mp=241–243 °C; IR (cm^{-1}) υ_{max} 3367, 2923, 1621, 1512, 1476, 1440, 1237, 1075, 819, 743, 709, 685, 501; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.39 (br s, 2H, N*H*+N*H*), 8.51 (d, J=2.0 Hz, 1H, *H*-7), 8.07 (d, J=8.7 Hz, 1H, *H*-4), 7.95 (d, J=7.2 Hz, 2H, *H*-Ph), 7.84 (s, 1H, $H_{thiazole}$), 7.77 (dd, J=8.7, 2.0 Hz, 1H, *H*-5), 7.48 (t, J=7.5 Hz, 2H, *H*-Ph), 7.37 (t, J=7.3 Hz, 1H, *H*-Ph); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.0, 166.6, 152.7, 151.7, 151.5, 138.8, 134.5, 130.8, 129.4 (2C), 128.6, 126.3 (2C), 125.9, 125.7, 120.3, 110.7; HRMS calcd for $C_{17}H^{79}_{12}BrN_4S_2$ $[M+H]^+$ 414.9687, found 414.9685.

*4.6.7. 6-Bromo-N-(4-p-tolylthiazol-2-yl)benzo[d]thiazole-2-carboximidamide (**25**).* Yield 74% (0.635 g), yellow solid, mp=265–267 °C; IR (cm^{-1}) υ_{max} 3369, 2927, 1620, 1599, 1511, 1476, 1441, 1301, 1236, 1117, 1049, 858, 817, 736, 491; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.38 (br s, 2H, N*H*+N*H*), 8.52 (d, J=1.9 Hz, 1H, *H*-7), 8.08 (d, J=8.7 Hz, 1H, *H*-4), 7.84 (d, J=8.1 Hz, 2H, *H*-Ph), 7.79 (d, J=2.0 Hz, 1H, *H*-5), 7.77 (s, 1H, $H_{thiazole}$), 7.28 (d, J=8.0 Hz, 2H, *H*-Ph), 2.35 (s, 3H, Ph-CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 172.9, 166.6, 152.7, 151.8, 151.4, 138.8, 138.1, 131.9, 130.8, 130.0 (2C), 126.2 (2C), 125.9, 125.7, 120.3, 109.9, 20.8; HRMS calcd for $C_{18}H^{79}_{14}BrN_4S_2$ $[M+H]^+$ 428.9843, found 428.9864.

*4.6.8. 6-Bromo-N-[4-(4-methoxyphenyl)thiazol-2-yl]benzo[d]-thiazole-2-carboximidamide (**26**).* Yield 82% (0.730 g), yellow solid, mp=243–245 °C; IR (cm^{-1}) υ_{max} 3460, 3247, 3067, 2955, 1609, 1519, 1479, 1250, 1232, 831, 735, 693; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.36 (br s, 2H, N*H*+N*H*), 8.51 (d, J=2.0 Hz, 1H, *H*-7), 8.07 (d, J=8.7 Hz, 1H, *H*-4), 7.87 (d, J=8.8 Hz, 2H, *H*-Ph), 7.77 (dd, J=8.7, 2.0 Hz, 1H, *H*-5), 7.66 (s, 1H, $H_{thiazole}$), 7.03 (d, J=8.8 Hz, 2H, *H*-Ph), 3.80 (s, 3H, Ph-OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 172.9, 166.6, 160.0, 152.7, 151.6, 151.4, 138.8, 130.8, 127.7 (2C), 127.3, 125.9, 125.7, 120.3, 114.7 (2C), 108.7, 55.3; HRMS calcd for $C_{18}H^{79}_{14}BrN_4OS_2$ $[M+H]^+$ 444.9792, found 444.9792.

*4.6.9. 6-Bromo-N-(4-(4-chlorophenyl)thiazol-2-yl)benzo[d]-thiazole-2-carboximidamide (**27**).* Yield 65% (0.583 g), yellow solid, mp=>300 °C; IR (cm^{-1}) υ_{max} 3368, 2923, 1620, 1584, 1542, 1509, 1471, 1401, 1305, 1237, 1094, 1012, 861, 819, 734, 487; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.34 (br s, 2H, N*H*+N*H*), 8.51 (d, J=2.0 Hz, 1H, *H*-7), 8.07 (d, J=8.7 Hz, 1H, *H*-4), 7.98 (d, J=8.6 Hz, 2H, *H*-Ph), 7.90 (s, 1H, $H_{thiazole}$), 7.77 (dd, J=8.7, 2.0 Hz, 1H, *H*-5), 7.53 (d, J=8.6 Hz, 2H, *H*-Ph); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.1, 166.5, 152.7, 151.5, 150.5, 138.8, 133.4, 133.1, 130.8, 129.4 (2C), 128.1 (2C), 125.9, 125.7, 120.3, 111.4; HRMS calcd for $C_{17}H^{79}_{11}BrClN_4S_2$ $[M+H]^+$ 448.9297, found 448.9293.

*4.6.10. 6-Bromo-N-(4-(2,4-dichlorophenyl)thiazol-2-yl)benzo[d]-thiazole-2-carboximidamide (**28**).* Yield 33% (0.317 g), yellow solid, mp=225–227 °C; IR (cm^{-1}) υ_{max} 3365, 3247, 3202, 1620, 1579, 1542, 1507, 1464, 1377, 1298, 1242, 1107, 1042, 865, 809, 747, 481; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.39 (br s, 2H, N*H*+N*H*), 8.53 (d, J=2.0 Hz, 1H, *H*-7), 8.07 (d, J=8.7 Hz, 1H), 7.89 (d, J=8.4 Hz, 1H, *H*-Ph), 7.81 (s, 1H, $H_{thiazole}$), 7.80–7.75 (m, 2H, H_{ar}+*H*-Ph), 7.56 (dd, J=8.4, 2.2 Hz, 1H, *H*-Ph); ^{13}C NMR (75 MHz, DMSO-d_6) δ 172.4, 166.5, 152.7, 151.8, 147.5, 138.8, 133.9, 133.1, 132.5, 132.4, 130.8, 130.5, 128.3, 126.0, 125.8, 120.4, 116.0; HRMS calcd for $C_{17}H^{79}_{10}BrCl_2N_4S_2$ $[M+H]^+$ 482.8907, found 482.8906.

*4.6.11. N-(4-Phenylthiazol-2-yl)thiazolo[5,4-b]pyridine-2-carbo-ximidamide (**29**).* Yield 56% (0.374 g), yellow solid, mp=221–223 °C; IR (cm^{-1}) υ_{max} 3359, 3185, 3056, 1624, 1476, 1439, 1235, 803, 7716, 682, 495; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.41 (br s, 2H, N*H*+N*H*), 8.76 (dd, J=4.6, 1.5 Hz, 1H, *H*-6), 8.55 (dd, J=8.3, 1.5 Hz, 1H, *H*-4), 8.02–7.91 (m, 2H, *H*-Ph), 7.87 (s, 1H, $H_{thiazole}$), 7.70 (dd, J=8.3, 4.6 Hz, 1H, *H*-5), 7.48 (t, J=7.5 Hz, 2H, *H*-Ph), 7.37 (t, J=7.3 Hz, 1H, *H*-Ph); ^{13}C NMR (75 MHz, DMSO-d_6) δ 172.9, 165.6, 159.1, 151.7, 151.4, 149.8, 146.8, 134.5, 131.9, 129.4 (2C), 128.6, 126.3 (2C), 123.0, 110.9; HRMS calcd for $C_{16}H_{12}N_5S_2$ $[M+H]^+$ 338.0534, found 338.0523.

*4.6.12. N-(4-p-Tolylthiazol-2-yl)thiazolo[5,4-b]pyridine-2-carbo-ximidamide (**30**).* Yield 63% (0.464 g), yellow solid, mp=233–235 °C; IR (cm^{-1}) υ_{max} 3298, 3163, 3112, 2927, 1618, 1498, 1476, 1443, 1224,

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795, 741, 615, 591; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.51 (br s, 1H, N*H*), 9.27 (br s, 1H, N*H*), 8.75 (dd, *J*=4.6, 1.4 Hz, 1H, *H*-6), 8.54 (dd, *J*=8.3, 1.4 Hz, 1H, *H*-4), 7.84 (d, *J*=8.1 Hz, 2H, *H*-Ph), 7.78 (s, 1H, $H_{thiazole}$), 7.69 (dd, *J*=8.3, 4.6 Hz, 1H, *H*-5), 7.28 (d, *J*=8.1 Hz, 2H, *H*-Ph), 2.34 (s, 3H, Ph-CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 172.8, 165.6, 159.1, 151.8, 151.3, 149.8, 146.8, 138.1, 131.9, 131.8, 130.0 (2C), 126.2 (2C), 123.0, 110.1, 20.8; HRMS calcd for $C_{17}H_{14}N_5S_2$ $[M+H]^+$ 352.0691, found 352.0688.

*4.6.13. N-[4-(4-Methoxyphenyl)thiazol-2-yl]thiazolo[5,4-b]pyridine-2-carboximidamide (**31**).* Yield 63% (0.463 g), yellow solid, mp=248–250 °C; IR (cm^{-1}) υ_{max} 3291, 3225, 3105, 3055, 2993, 1610, 1527, 1476, 1445, 1248, 1225, 8832, 739, 616, 579; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.57 (br s, 1H, N*H*), 9.27 (br s, 1H, N*H*), 8.76 (dd, *J*=4.6, 1.5 Hz, 1H, *H*-6), 8.55 (dd, *J*=8.3, 1.5 Hz, 1H, *H*-4), 7.89 (d, *J*=8.8 Hz, 2H, *H*-Ph), 7.77–7.64 (m, 2H, *H*-5+$H_{thiazole}$), 7.04 (d, *J*=8.8 Hz, 2H, *H*-Ph), 3.81 (s, 3H, Ph-OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 172.8, 165.7, 160.0, 159.2, 151.7, 151.3, 149.8, 146.9, 132.0, 127.8 (2C), 127.3, 123.1, 114.7 (2C), 108.9, 55.3; HRMS calcd for $C_{17}H_{14}N_5OS_2$ $[M+H]^+$ 368.0640, found 368.0644.

*4.6.14. N-[4-(4-Chlorophenyl)thiazol-2-yl]thiazolo[5,4-b]pyri-dine-2-carboximidamide (**32**).* Yield 38% (0.280 g), yellow solid, mp=264–266 °C; IR (cm^{-1}) υ_{max} 3309, 3235, 3173, 3128, 3054, 1620, 1536, 1503, 1469, 1226, 829, 733, 613; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.38 (br s, 2H, N*H*+N*H*), 8.76 (dd, *J*=4.6, 1.5 Hz, 1H, H-6), 8.55 (dd, *J*=8.3, 1.5 Hz, 1H, H-4), 7.99 (d, *J*=8.6 Hz, 2H, *H*-Ph), 7.92 (s, 1H, $H_{thiazole}$), 7.70 (dd, *J*=8.3, 4.6 Hz, 1H, H-5), 7.53 (d, *J*=8.6 Hz, 2H, *H*-Ph); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.1, 165.6, 159.2, 151.4, 150.6, 149.9, 146.8, 133.4, 133.2, 132.0, 129.4 (2C), 128.1 (2C), 123.1, 111.7; HRMS calcd for $C_{16}H_{11}ClN_5S_2$ $[M+H]^+$ 372.0144, found 372.0131.

*4.6.15. N-[4-(2,4-Dichlorophenyl)thiazol-2-yl]thiazolo[5,4-b]-pyridine-2-carboximidamide (**33**).* Yield 47% (0.382 g), yellow solid, mp=242–246 °C; IR (cm^{-1}) υ_{max} 3438, 3314, 3163, 3067, 1619, 1498, 1465, 1373, 1228, 1140, 867, 798, 738; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.40 (br s, 2H, N*H*+N*H*), 8.76 (dd, *J*=4.6, 1.5 Hz, 1H, *H*-6), 8.54 (dd, *J*=8.3, 1.5 Hz, 1H, *H*-4), 7.89 (d, *J*=8.4 Hz, 1H, *H*-Ph), 7.83 (s, 1H, $H_{thiazole}$), 7.76 (d, *J*=2.2 Hz, 1H, *H*-Ph), 7.70 (dd, *J*=8.3, 4.6 Hz, 1H, *H*-5), 7.56 (dd, *J*=8.4, 2.2 Hz, 1H, *H*-Ph); ^{13}C NMR (75 MHz, DMSO-d_6) δ 172.3, 165.5, 159.1, 151.7, 149.9, 147.5, 146.8, 133.9, 133.1, 132.5, 132.4, 132.0, 130.5, 128.3, 123.1, 116.2; HRMS calcd for $C_{16}H_{10}Cl_2N_5S_2$ $[M+H]^+$ 405.9755, found 405.9756.

*4.6.16. N-(4-p-Tolylthiazol-2-yl)thiazolo[4,5-b]pyridine-2-carbo-ximidamide (**34**).* Yield 58% (0.411 g), yellow solid, mp=286–288 °C; IR (cm^{-1}) υ_{max} 3381, 3271, 3094, 1613, 1541, 1518, 1475, 1227, 1109, 1028, 862, 777, 744, 629; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.48 (br s, 2H, N*H*+N*H*), 8.83 (dd, *J*=4.6, 1.5 Hz, 1H, *H*-5), 8.72 (dd, *J*=8.1, 1.5 Hz, 1H, *H*-7), 7.85 (d, *J*=8.1 Hz, 2H, *H*-Ph), 7.78 (s, 1H, $H_{thiazole}$), 7.60 (dd, *J*=8.1, 4.6 Hz, 1H, *H*-6), 7.29 (d, *J*=8.0 Hz, 2H, *H*-Ph), 2.31 (s, 3H, Ph-CH_3); HRMS calcd for $C_{17}H_{14}N_5S_2$ $[M+H]^+$ 352.0691, found 352.0692.

*4.6.17. N-[4-(2,4-Dichlorophenyl)thiazol-2-yl]thiazolo[4,5-b]-pyridine-2-carboximidamide (**35**).* Yield 77% (0.566 g), yellow solid, mp=290–292 °C; IR (cm^{-1}) υ_{max} 3378, 3236, 3185, 2916, 1608, 1519, 1479, 1450, 1244, 1173, 1023, 818, 779; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.49 (br s, 2H, N*H*+N*H*), 8.82 (dd, *J*=4.5, 1.3 Hz, 1H, *H*-5), 8.72 (dd, *J*=8.1, 1.3 Hz, 1H, *H*-7), 7.89 (d, *J*=8.7 Hz, 2H, *H*-Ph), 7.69 (s, 1H, $H_{thiazole}$), 7.60 (dd, *J*=8.1, 4.5 Hz, 1H, *H*-6), 7.04 (d, *J*=8.7 Hz, 2H, *H*-Ph), 3.81 (s, 3H, Ph-OCH_3) HRMS calcd for $C_{17}H_{14}N_5OS_2$ $[M+H]^+$ 368.0640, found 368.0642.

*4.6.18. N-(4-Phenylthiazol-2-yl)benzo[d]oxazole-2-carboximidamide (**36**).* Yield 51% (0.327 g), light yellow solid, mp=235–237 °C; IR (cm^{-1}) υ_{max} 3343, 1633, 1599, 1560, 1529, 1476, 1437, 1406, 1227, 1174, 1069, 907, 859, 814, 725, 692, 664, 627, 507; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.44 (br s, 2H, N*H*+N*H*), 7.98–7.89 (m, 4H, H_{ar}), 7.86 (s, 1H, $H_{thiazole}$), 7.63–7.44 (m, 4H, *H*-Ph), 7.37 (t, *J*=7.3 Hz, 1H, *H*-Ph); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.3, 158.0, 151.6, 151.3, 146.9, 141.0, 134.5, 129.4 (2C), 128.6, 127.9, 126.3 (2C), 126.1, 121.2, 112.2, 111.0; HRMS calcd for $C_{17}H_{13}N_4OS$ $[M+H]^+$ 321.0810, found 321.0799.

*4.6.19. N-(4-p-Tolylthiazol-2-yl)benzo[d]oxazole-2-carboximidamide (**37**).* Yield 47% (0.314 g), light yellow solid, mp=246–248 °C; IR (cm^{-1}) υ_{max} 3349, 1633, 1602, 1558, 1530, 1477, 1408, 1225, 1172, 824, 740, 732, 696, 616, 498; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.43 (br s, 2H, N*H*+N*H*), 7.95–7.89 (m, 2H, H_{ar}), 7.84 (d, *J*=8.1 Hz, 2H, *H*-Ph), 7.78 (s, 1H, $H_{thiazole}$), 7.62–7.48 (m, 2H, H_{ar}), 7.28 (d, *J*=8.1 Hz, 2H, *H*-Ph), 2.35 (s, 3H, Ph-CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 172.4, 157.3, 151.0, 150.5, 146.1, 140.4, 137.4, 131.3, 129.3 (2C), 127.3, 125.7 (2C), 125.5, 120.6, 111.7, 109.7, 20.8; HRMS calcd for $C_{18}H_{15}N_4OS$ $[M+H]^+$ 335.0967, found 335.0975.

*4.6.20. N-[4-(4-Methoxyphenyl)thiazol-2-yl]benzo[d]oxazole-2-carboximidamide (**38**).* Yield 60% (0.420 g), light yellow solid, mp=216–218 °C; IR (cm^{-1}) υ_{max} 3393, 3185, 3112, 2977, 1627, 1603, 1523, 1479, 1237, 1174, 826, 766, 746, 528; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.42 (br s, 2H, N*H*+N*H*), 7.96–7.91 (m, 2H, H_{ar}), 7.88 (d, *J*=8.8 Hz, 2H, *H*-Ph), 7.69 (s, 1H, $H_{thiazole}$), 7.62–7.47 (m, 2H, H_{ar}), 7.03 (d, *J*=8.8 Hz, 2H, *H*-Ph), 3.81 (s, 3H, Ph-OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.2, 159.9, 158.1, 151.6, 151.3, 146.8, 141.0, 127.9, 127.7 (2C), 127.3, 126.1, 121.2, 114.7 (2C), 112.2, 109.0, 55.3; HRMS calcd for $C_{18}H_{15}N_4O_2S$ $[M+H]^+$ 351.0916, found 351.0904.

*4.6.21. N-(4-(4-Chlorophenyl)thiazol-2-yl)benzo[d]oxazole-2-carboximidamide (**39**).* Yield 62% (0.440 g), light yellow solid, mp=221–223 °C; IR (cm^{-1}) υ_{max} 3352, 1634, 1601, 1533, 1470, 1402, 1231, 1090, 737, 506; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.38 (br s, 2H, N*H*+N*H*), 7.99 (d, *J*=8.4 Hz, 2H, *H*-Ph), 7.95–7.89 (m, 3H, H_{ar}+*H*-$_{thiazole}$), 7.62–7.48 (m, 2H, H_{ar}), 7.53 (d, *J*=8.4 Hz, 1H, *H*-Ph); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.5, 158.0, 151.2, 150.4, 146.9, 141.0, 133.4, 133.1, 129.4 (2C), 128.1 (2C), 127.9, 126.1, 121.2, 112.2, 111.7; HRMS calcd for $C_{17}H_{12}ClN_4OS$ $[M+H]^+$ 355.0420, found 355.0437.

*4.6.22. N-[4-(2,4-Dichlorophenyl)thiazol-2-yl]benzo[d]oxazole-2-carboximidamide (**40**).* Yield 36% (0.280 g), light yellow solid, mp=253–255 °C; IR (cm^{-1}) υ_{max} 3361, 3203, 1636, 1604, 1537, 1464, 1232, 1103, 1042, 867, 755, 739; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.39 (br s, 2H, N*H*+N*H*), 7.94–7.87 (m, 3H, H_{ar}), 7.82 (s, 1H, $H_{thia-zole}$), 7.74 (d, *J*=2.1 Hz, 1H, *H*-Ph), 7.61–7.48 (m, 3H, H_{ar}); ^{13}C NMR (75 MHz, DMSO-d_6) δ 172.6, 157.9, 151.2, 147.4, 147.2, 141.0, 133.8, 133.0, 132.5, 132.3, 130.5, 128.2, 127.9, 126.1, 121.2, 116.3, 112.2; HRMS calcd for $C_{17}H_{11}C_{l2}N_4OS$ $[M+H]^+$ 389.0031, found 389.0025.

*4.6.23. 6-Bromo-N-(4-phenylthiazol-2-yl)benzo[d]oxazole-2-carboximidamide (**41**).* Yield 56% (0.451 g), yellow solid, mp=202–204 °C; IR (cm^{-1}) υ_{max} 3357, 2914, 1630, 1597, 1556, 1531, 1476, 1440, 1318, 1235, 1073, 1042, 907, 854, 814, 709, 489; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.42 (br s, 2H, N*H*+N*H*), 8.26 (d, *J*=1.6 Hz, 1H, *H*-7), 7.94 (d, *J*=7.5 Hz, 2H, *H*-Ph), 7.91–7.83 (m, 2H, *H*-4+$H_{thiazole}$), 7.68 (dd, *J*=8.5, 1.6 Hz, 1H, *H*-5), 7.47 (t, *J*=7.5 Hz, 2H, *H*-Ph), 7.36 (t, *J*=7.3 Hz, 1H, *H*-Ph); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.2, 158.6, 151.9, 151.7, 146.5, 140.4, 134.5, 129.4 (2C), 128.7, 126.3 (2C), 122.6, 120.0, 115.6, 111.2; HRMS calcd for $C_{17}H^{79}_{12}BrN_4OS$ $[M+H]^+$ 398.9915, found 398.9934.

*4.6.24. 6-Bromo-N-(4-p-tolylthiazol-2-yl)benzo[d]oxazole-2-carboximidamide (**42**).* Yield 51% (0.430 g), yellow solid, mp=226–228 °C; IR (cm^{-1}) υ_{max} 3351, 3178, 3077, 1631, 1599, 1553,

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1530, 1476, 1412, 1237, 812, 729; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.94 (br s, 2H, N*H*+N*H*), 7.78 (s, 1H, *H*-7), 7.43–7.26 (m, 4H, *H*-4+$H_{thiazole}$+*H*-Ph), 7.20 (d, *J*=8.5 Hz, 1H, *H*-5), 6.78 (d, *J*=7.8 Hz, 2H, *H*-Ph), 1.85 (s, 3H, Ph-CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.1, 158.6, 151.9, 151.8, 146.5, 140.4, 138.1, 131.9, 130.0 (2C), 129.4, 126.3 (2C), 122.7, 120.0, 115.7, 110.4, 20.8; HRMS calcd for $C_{18}H_{14}^{79}BrN_4OS$ $[M+H]^+$ 413.0072, found 413.0078.

*4.6.25. 6-Bromo-N-[4-(4-methoxyphenyl)thiazol-2-yl]benzo[d]-oxazole-2-carboximidamide (**45**).* Yield 52% (0.429 g), yellow solid, mp=223–225 °C; IR (cm^{-1}) υ_{max} 3391, 3190, 3105, 1628, 1598, 1525, 1477, 1412, 1239, 1175, 1112, 1017, 820, 743, 533; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.43 (br s, 2H, N*H*+N*H*), 8.27 (d, *J*=1.6 Hz, 1H, *H*-7), 7.91–7.86 (m, 3H,*H*-4+*H*-Ph), 7.73–7.66 (m, 2H, *H*-5+$H_{thiazole}$), 7.03 (d, *J*=8.8 Hz, 2H, *H*-Ph), 3.80 (s, 3H, Ph-OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.1, 160.0, 158.6, 151.9, 151.7, 146.5, 140.4, 129.4, 127.7 (2C), 127.3, 122.7, 120.0, 115.7, 114.7 (2C), 109.2, 55.3; HRMS calcd for $C_{18}H_{14}^{79}BrN_4O_2S$ $[M+H]^+$ 429.0021, found 429.0024.

*4.6.26. 6-Bromo-N-(4-(4-chlorophenyl)thiazol-2-yl)benzo[d]oxazole-2-carboximidamide (**44**).* Yield 44% (0.382 g), yellow solid, mp=230–232 °C; IR (cm^{-1}) υ_{max} 3356, 3202, 3107, 1632, 1599, 1534, 1470, 1402, 1234, 1094, 1064, 1013, 911, 859, 824, 737, 488; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.40 (br s, 2H, N*H*+N*H*), 8.27 (d, *J*=1.5 Hz, 1H, *H*-7), 7.98 (d, *J*=8.5 Hz, 2H, *H*-Ph), 7.93 (s, 1H, $H_{thiazole}$), 7.88 (d, *J*=8.5 Hz, 1H, *H*-4), 7.69 (dd, *J*=8.5, 1.5 Hz, 1H, *H*-5), 7.52 (d, *J*=8.5 Hz, 2H, *H*-Ph); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.3, 158.6, 154.7, 151.9, 150.5, 146.6, 140.4, 133.4, 133.1, 129.4 (2C), 128.1 (2C), 122.7, 120.0, 115.7, 112.0; HRMS calcd for $C_{17}H_{11}^{79}BrClN_4OS$ $[M+H]^+$ 432.9525, found 432.9533.

*4.6.27. 6-Bromo-N-(4-(2,4-chlorophenyl)thiazol-2-yl)benzo[d]-oxazole-2-carboximidamide (**45**).* Yield 42% (0.462 g), yellow solid, mp=211–213 °C; IR (cm^{-1}) υ_{max} 3440, 3235, 3100, 1622, 1595, 1554, 1516, 1465, 1238, 1104, 1043, 909, 863, 810, 757; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.41 (br s, 2H, N*H*+N*H*), 8.25 (d, *J*=1.7 Hz, 1H, *H*-7), 7.88 (d, *J*=8.4 Hz, 1H, *H*-Ph), 7.86 (d, *J*=8.5 Hz, 1H, *H*-4), 7.83 (s, 1H, $H_{thiazole}$), 7.74 (d, *J*=2.1 Hz, 1H, *H*-Ph), 7.67 (dd, *J*=8.5, 1.7 Hz, 1H, *H*-5), 7.54 (dd, *J*=8.4, 2.1 Hz, 1H, *H*-Ph); ^{13}C NMR (75 MHz, DMSO-d_6) δ 172.5, 158.5, 151.9, 147.4, 146.8, 140.4, 133.8, 133.0, 132.5, 132.3, 130.5, 129.4, 128.3, 122.6, 120.0, 116.4, 115.7; HRMS calcd for $C_{17}H_{10}^{79}BrCl_2N_4OS$ $[M+H]^+$ 466.9136, found 466.9125.

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Supplementary data

^{1}H and ^{13}C NMR spectra of all compounds are available. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2014.06.102.

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