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Ru(II)-Catalyzed Regioselective C−N Bond Formation on Benzothiazoles Employing Acyl Azide as an Amidating Agent

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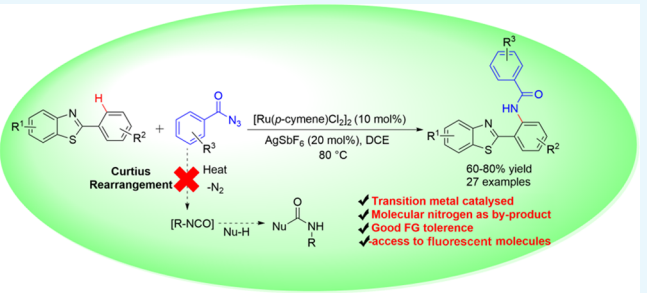
ABSTRACT: A Ru(II)-catalyzed regioselective direct *ortho*-amidation of 2-aryl benzo[*d*]thiazoles employing acyl azides as a nitrogen source has been accomplished. This approach utilizes the efficiency of benzothiazole as a directing group and the role of acyl azide as an effective amidating agent toward C−N bond formation, thereby evading the general Curtius rearrangement. The protocol highlights significant functional group tolerance, single-step, and external oxidant-free conditions, with the release of only innocuous molecular nitrogen as the byproduct. The reaction mechanism and the intermediates associated with this selective Ru-catalyzed reaction have been investigated using ESI-MS. The protocol also aided in the construction of *ortho*-amidated *β*-carbolines, unveiling another class of fluorescent molecules.



INTRODUCTION

C−H functionalization has proved to be a sustainable alternative approach in synthetic chemistry. This includes introducing functional groups (C, O, N, S, and halides),[1a] biaryl coupling,[1b,c] or cyclizations[1d,e] with superior chemo-, regio-, and stereoselectivity. Transition metal-catalyzed C−H functionalization has occupied a prominent position in modern synthetic chemistry due to its extreme precision in constructing carbon−heteroatom bonds in an atom-economic way. Over the past few decades, various C−X (X = O, S, and N)[2] bond formation reactions have been studied and utilized for diverse synthetic metamorphosis. Among them, the C−N bond has garnered considerable attention from organic chemists due to its presence in various naturally and pharmaceutically important molecules such as capsaicin, penicillin, and paracetamol. Utilization of a directing group acts as a promising strategy in achieving high selectivity due to coordination of the transition metal with the heteroatom of the directing group, which leads to the activation of the proximal C−H bond via chelation assistance.[3]

Over time, most of the reports on functionality derived reactions such as *ortho*-acylation, alkenylation, arylation, cyanation, hydroxylation, sulfonation, nitration, acetoxylation, halogenation, and amidation have delineated the use of benzothiazoles as an effective directing group.[4] The prevalence of benzothiazole scaffolds in various natural products with eminent pharmacological activity and efficiency as a directing group has placed them at the forefront of chemical research. They possess vivid biological activities such as anti-tumor (**I**),[5] anti-hepatitis C,[6] anti-Alzheimer,[7] anti-inflammatory, analgesic,[8] and anti-oxidant (**II**).[9] The adept fluorescent nature of benzothiazole-based molecules represents a class of heterocycles with efficient white light emission[10] and chemosensor[11] (**III** and **IV**) ability (Figure 1). In recent times, white organic light-emitting diodes (WOLEDs) have drawn considerable

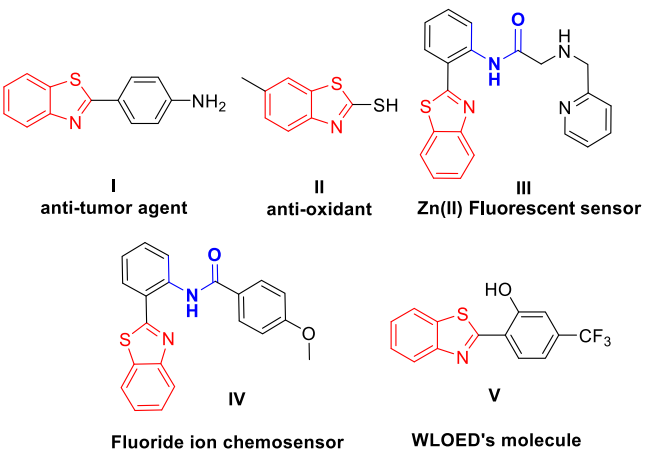


Figure 1. Benzothiazole-containing molecules.

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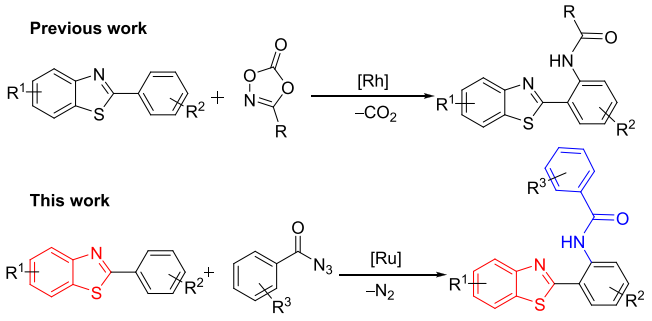
attention with prominent application in the field of flat panel displays, lighting equipment, and so on.[12] There are many competent methods described for white light emission.[13] A newer addition to this category is the use of single organic molecules as white light emitters with added advantages over the others, such as good reproducibility, simple fabrication process, and improved stability. Benzothiazole-based molecules have been well established as significant molecules in the field of WOLEDs (**V**), making them a moiety of particular interest (Figure 1).

Therefore, efficient synthetic approaches for the functionalized benzothiazoles are highly desired to explore their potential applications. An extensive abundance of carbamide functionality in biologically important molecules advocates the importance of amide linkage. Amide linkages enhance the molecule's interaction with an increased probability of hydrogen bonding when compared in the absence of an amide bond. Synthesis of bioactive molecules by amide incorporation has been one of the most significant organic manipulations undertaken by researchers globally.[14] C−N bond formation aided by transition metal[15] has efficiently assisted the need for synthetic methodologies for selective synthesis of carbamide-containing molecules. Various substrates such as *N*-tosylates,[16] dioxazolones,[17] amides,[18] carbamates,[19] and others[20] have been successfully employed as amidating reagents. Ding et al. reported Rh-catalyzed 2-arylbenzo[*d*]thiazole C−H amidation using dioxazolone as an amidating agent[17c] (Scheme 1). On the other hand, acyl azides

Scheme 1. Methods for *o*-Amidation of 2-Aryl Benzothiazoles

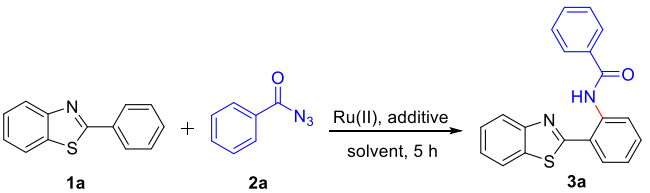


have been employed in the facile formation of C−C bonds in various moieties[21] via in situ generation of isocyanates. Chang et al. explored the dual reactivity of acyl azide to facilitate C−N and C−C amidation based on the catalytic system.[22] This was followed by acyl azide-mediated C−N amide formation utilizing Cu,[23a,b] Ir,[23c,d] Ru,[23e] and Co[23f] transition metal catalysts. Acyl azides are readily prepared, and their broad-spectrum utilization in selective amidation in the presence of less-expensive catalysts is highly desirable. With only handful of such results, acyl azides can be an interesting approach toward amidation strategy. Therefore, in continuation of our efforts[24] toward the development of transition metal-catalyzed C−H activation, herein, we report a Ru(II)-catalyzed regioselective construction of the C−N bond on benzothiazoles using acyl azide as an amidating agent (Scheme 1).

RESULTS AND DISCUSSION

The key substrates **1a**−**o** and **2a**−**l** were primarily synthesized according to the previous reports.[25] The reaction was commenced with a model reaction between 2-phenylbenzo[*d*]thiazole (**1a**) and acyl azide (**2a**) as an amidating agent employing $[Ru(p\text{-cymene})Cl_2]_2$ (5 mol %) and $AgSbF_6$ (20 mol %) as additives in DCE at 80 °C. To our delight, the desired product **3a** was obtained in 50% yield (entry 1, Table 1). Encouraged by the desired result, we further aimed at

Table 1. Optimization of the Reaction Conditions for C−H Activation[a]



entry	catalyst (5 mol %)	additive	solvent	yield (%)
1	$[Ru(p\text{-cymene})Cl_2]_2$	$AgSbF_6$	DCE	50
2	$[Ru(p\text{-cymene})Cl_2]_2$	$Cu(OAc)_2$	DCE	20
3	$[Ru(p\text{-cymene})Cl_2]_2$	$Ag(OAc)_2$	DCE	30
4	$[Ru(p\text{-cymene})Cl_2]_2$	TBAI	DCE	NR
5	$[Ru(p\text{-cymene})Cl_2]_2$	O_2	DCE	trace
6	$[Ru(p\text{-cymene})Cl_2]_2$	Ag_2CO_3	DCE	NR
7	$[Ru(p\text{-cymene})Cl_2]_2$	AgOTf	DCE	25
8	$[Ru(p\text{-cymene})Cl_2]_2$	$Cu(OAc)_2$	Toluene	10[b]
9	$[Ru(p\text{-cymene})Cl_2]_2$	$AgSbF_6$	Toluene	45[b]
10	$[Ru(p\text{-cymene})Cl_2]_2$	$AgSbF_6$	1,4-dioxane	35[c]
11	$[Ru(p\text{-cymene})Cl_2]_2$	$AgSbF_6$	CH_3CN	10
12	$[Ru(p\text{-cymene})Cl_2]_2$	$AgSbF_6$	EtOH	NR
13	$[Ru(p\text{-cymene})Cl_2]_2$	$AgSbF_6$	DCE	70[d]
14	$[Ru(p\text{-cymene})Cl_2]_2$		DCE	trace
15	$Pd(OAc)_2$	$Cu(OAc)_2$	CH_3CN	NR
16	$CoCl_2$	PIDA	DCE	NR
17	$[RhCp^*Cl_2]_2$	$AgSbF_6$	DCE	20

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (5 mol %), additive (20 mol %), solvent (2 mL), 80 °C, and 5 h in the pressure tube. [b]At 110 °C. [c]At 100 °C. [d]Catalyst (10 mol %). NR = no reaction.

enhancing the yield of product **3a** by scrutinizing different additives such as $Cu(OAc)_2$, $Ag(OAc)_2$, TBAI, O_2, Ag_2CO_3, and AgOTf (entries 2−7, Table 1). Additionally, a different combination of additive $Cu(OAc)_2$ with toluene as a solvent at higher temperature was also examined, but disappointingly, no increase in product yield was observed (entry 8, Table 1). This prompted us to shift our focus to the solvents used in the reaction. We screened the reaction in various solvent systems such as toluene, 1,4-dioxane, ACN, and EtOH and realized that DCE was the best for the reaction (entries 9−12, Table 1). An increase in the catalyst loading from 5 to 10 mol % invariably enhanced the product **3a** yield to 70% (entry 13, Table 1). The formation of a trace amount of product **3a** in the absence of $AgSbF_6$ indicated the significance of the additive for the reaction (entry 14, Table 1). A change in the catalytic system employing $Pd(OAc)_2$ and $CoCl_2$ with $Cu(OAc)_2$ and PIDA as additives, respectively, failed to produce the desired product **3a** (entries 15−16, Table 1). The reaction system in the presence of the Rh(III) catalyst with $AgSbF_6$ as an additive delivered only 20% yield of the desired product (entry 17, Table 1).

With the optimized reaction conditions, we further investigated the substrate scope of the protocol using various

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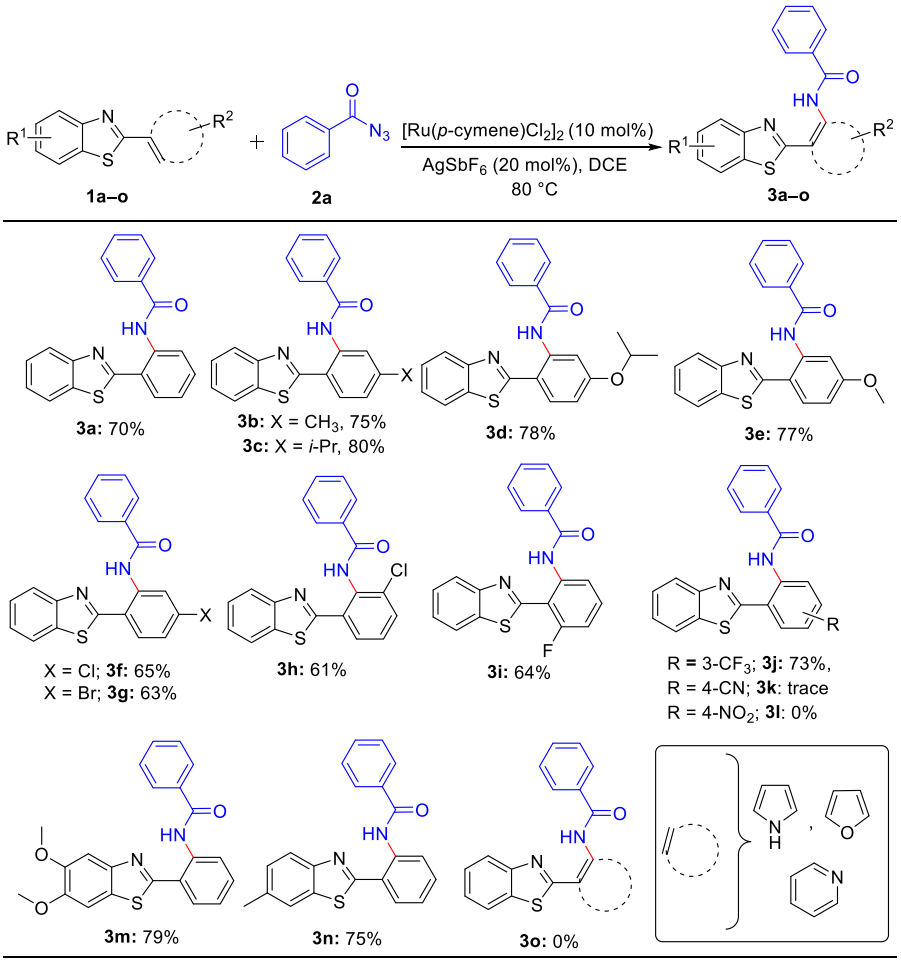
Table 2. Ru-Catalyzed Regioselective *o*-Amidation of 2-Arylbenzo[*d*]thiazoles[a]



[a]Reaction conditions: **1** (1 equiv), **2a** (1.5 equiv), [Ru(*p*-cymene)Cl_2]$_2$ (10 mol %), $AgSbF_6$ (20 mol %), DCE (2 mL), 80 °C, and 5−7 h in the pressure tube.

substituted 2-arylbenzo[*d*]thiazoles to explore the suitability of the protocol. All the substrates proved to produce the desired *ortho*-amidated products **3a−j** and **3m**, **n** in moderate to good yields. Substrates with substitution at the para-position (methyl, isopropyl, isopropoxy, and methoxy) of **1b−e** yielded the expected products **3b−e** in good yields (75−80%, Table 2). The *para*-halogenated substrates (chloro- and bromo-) **1f** and **1g** also afforded the desired products **3f** and **3g** in 65 and 63% yield, respectively. We also studied the effect of the substitution position and gratifyingly found that the *meta*-(chloro-) **1h** and *ortho*-position (fluoro) **1i** did not deter the product formation and resulted in **3h** and **3i**, respectively, in moderate yields (61 and 64%, respectively, Table 2). For unveiling the effect of EWG on the reaction results, we subjected *meta*-substituted trifluoromethyl and 4-CN- and 4-NO_2-substituted substrates and realized that 3-CF_3 delivered amidated product **3j** in 73% yield. Disappointingly, 4-CN showed only a trace amount of product **3k** formation, whereas the 4-NO_2 substitution failed to produce the desired product **3l**. Various substitution patterns on the benzene ring of benzothiazoles were found to be compatible with the reaction conditions and therefore afforded **3m** and **3n** in moderate yields (79 and 75%, respectively, Table 2). Disappointingly, replacing the 2-phenyl ring with the hetero-aromatic system failed to produce the *ortho*-amidated product **3o**, limiting the set protocol.

Subsequently, we shifted our attention toward exploring the protocol for C−H amidation of 2-aryl benzo[*d*]thiazoles with substituted acyl azides. Delightfully, the optimized condition utilizing substituted acyl azides as the amide source favored the formation of the desired products **3p−ae** in moderate to good yields. The study about the effect of electron-donating substitutions (4-OCH_3 and 4-CH_3) on acyl azides coupled with substituted 2-aryl benzothiazoles satisfactorily furnished the desired products **3p−t** (65−80%, Table 3).

The trimethoxy-substituted acyl azides also underwent the reaction smoothly and produced **3u** in 78% yield. The electron-withdrawing acyl azide (4-NO_2) did not affect the reaction results and delivered **3v** in 70% yield. Furthermore, a study with mono- and di-halogenated acyl azides (3-I and 3,5-diCl) also enabled access to the amidated products **3w−ad** in moderate yields (60−72%, Table 3). Additionally, an understanding of the substrate scope revealed the utility of the optimized condition in employing cinnamoyl azide to afford the target molecule **3ae** in a moderate yield of 60%. In our attempt to further decipher the scope of acyl azide, we employed hetero-aromatics such as 3-indole acyl azide, *N*-methyl 3-indole acyl azide, and picolinic acyl azide; however, it was observed that these acyl azides along with the aliphatic acyl

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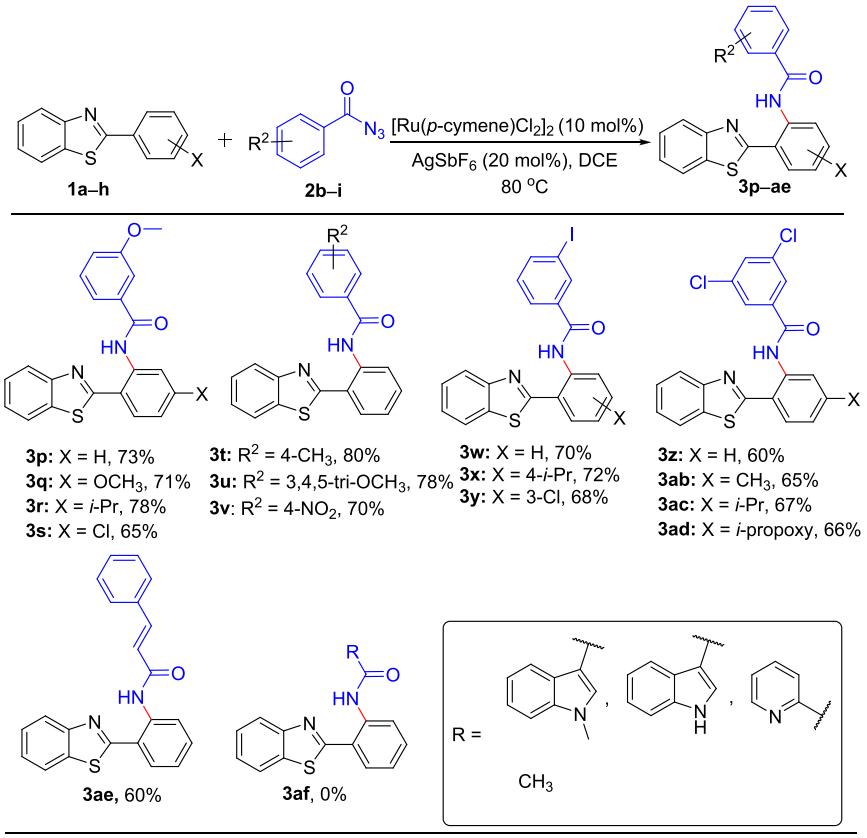
Table 3. Ru-Catalyzed Regioselective *o*-Amidation of 2-Arylbenzo[*d*]thiazoles with Substituted Acyl Azides[a]



[a]Reaction conditions: **1a** (1 equiv), **2** (1.5 equiv), $[Ru(p\text{-cymene})Cl_2]_2$ (10 mol %), $AgSbF_6$ (20 mol %), DCE (2 mL), 80 °C, and 5−7 h in the pressure tube.

azide (acetyl azide) failed to construct the desired molecules of interest (**3af**, Table 3).

Based on the previous reports[26] and with assistance of the ESI-MS technique wherein the intermediates were captured at varied time intervals to compile the MS data, a probable pathway for the reaction mechanism was determined. Figure 2a displays an ESI-MS spectrum of the reaction mixture after mixing **1a** and **2a**, the catalyst, and the additive in the reaction media, wherein *m*/*z* 212.0535 represents $[\mathbf{1a} + H]^+$. Furthermore, the reaction progress was observed after 5 min with the capturing of the five-membered ruthenacycle **A** with $[\mathbf{A}]^+$ at a *m*/*z* of 446.0511 (Figure 2b). After 30 min of reaction in the pressure tube, a peak at a *m*/*z* of 565.0849 appeared for **C** with $[\mathbf{C}]^+$, the transition metal complex characterized by the isotopic peak. A small peak accompanied this at a *m*/*z* of 331.0867, indicative of the product formation (Figure 2c). A further assessment of the reaction after 3 h revealed an increase in the intensity of the product peak compared to the substrate (Figure 2d).

With the aid of a previous report from the Punniyamurthy group[23e] and the ionization species identified from the abovementioned experiment, a probable mechanism is sketched in Scheme 2. The neutral precursor $[Ru(p\text{-cymene}Cl_2)]_2$ is activated to form the active cationic Ru(II) species in the presence of $AgSbF_6$. Next, a five-membered ruthenacycle species **A** is formed via C−H activation. The coordination of acyl azide (**2**) to intermediate **A** leads to ruthenium intermediate **B**. Furthermore, six-membered ruthenacycle species **C** formation is prompted by insertion of an amide moiety into the ruthenacycle followed by extrusion of the N_2 gas. Finally, the desired product **3** is generated by protonolysis along with active cationic ruthenium species regeneration.

Furthermore, we also performed an intermolecular competition experiment to compare the reactivity of varied azides, that is, **2d** (3,4,5-tri-OMe) and **2e** (4-NO_2) with **1a**. The results unveiled faster reaction of the **2e** azide than the electron-rich **2d** azide, which can be attributed to the greater stability of the electron-deficient acyl azide (Scheme 3).

To reveal the efficiency of the reaction at the gram-scale level, we coupled **1b** (4.44 mmol) with **2a** (6.66 mmol) and obtained amidated product **3b** in 78% yield. Further hydrolysis of **3b** afforded the free amine (**4**, 80% yield) at the *ortho*-position, which can be employed in synthetic transformations such as in the synthesis of *N*-benzylated benzothiazoles established as chemosensors for Hg^{2+} ions[27a] or the benzothiazole-tetraoxocalix[2]arene[2]triazine conjugates enabling cyanate detection[27b] (Scheme 4). Fascinatingly, in our pursuit to reconnoiter the application of our protocol, we strategized the development of amide linkage on biologically relevant *β*-carbolines **5**. To our delight, the established protocol encouragingly yielded *ortho*-amidated *β*-carbolines (**5a**,**b**) in 65 and 63% yield, respectively. The amidated *β*-carbolines exhibited florescent property[28] as depicted in Figure 3. Compound **5a** and **5b** demonstrated λ_{max} (excitation) at 275 nm and λ_{max} (emission) at 435 nm and λ_{max} (excitation) at 385 nm and λ_{max} (emission) at 566 nm, respectively.

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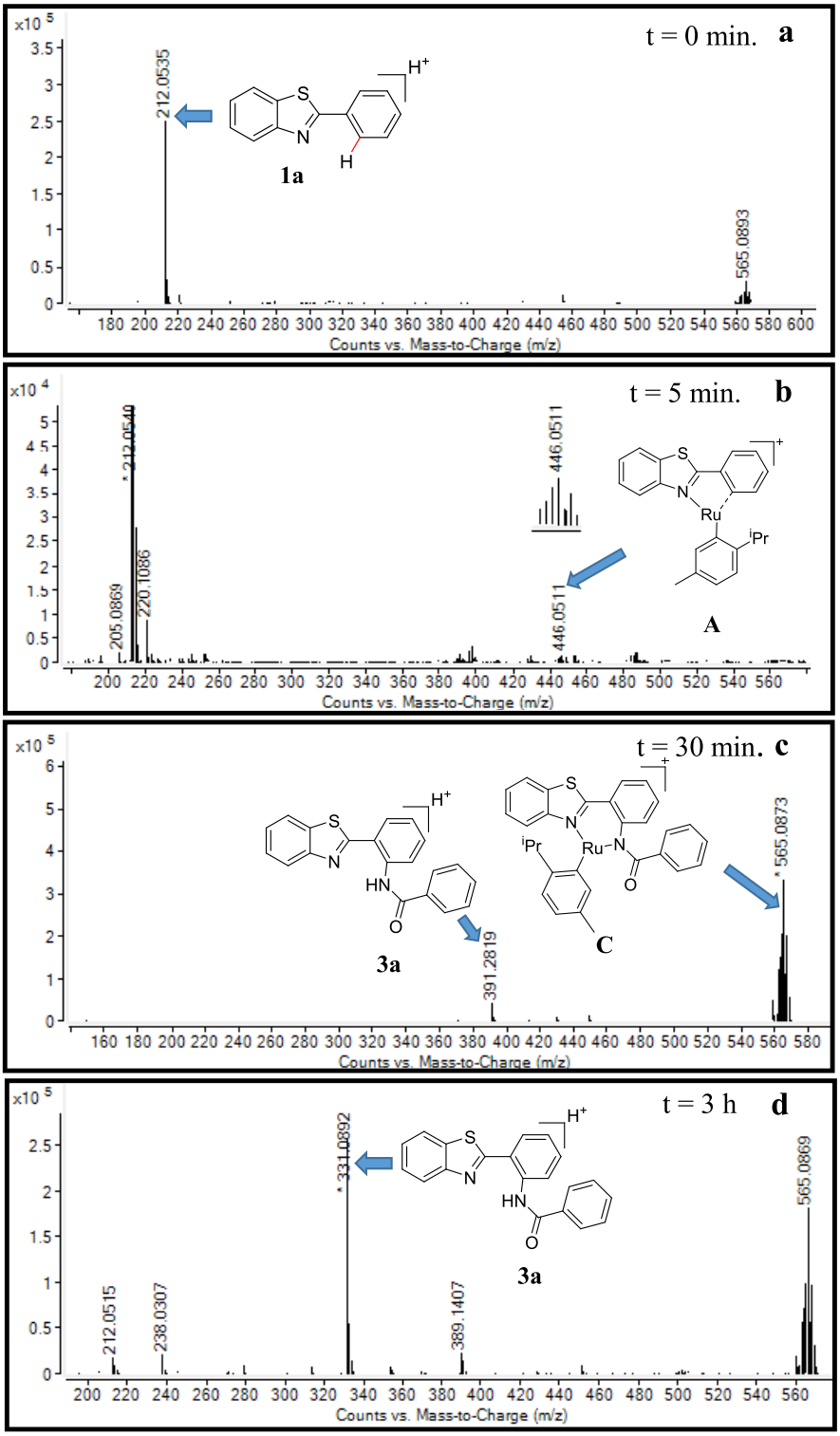

Figure 2. ESI-QTOF-MS monitoring of acyl azide-mediated amidation of **1a** at varied time intervals from 0.0 min to 3 h.

CONCLUSIONS

In summary, a protocol for *ortho*-amidation of 2-aryl benzothiazole in the presence of a Ru(II) catalyst via C−H activation was accomplished. The utility of acyl azide for the formation of a C−N bond was successfully explored, overcoming the intervention with isocyanate formation that might have led to a mixture of C−N and C−C amidated products. The mild reaction conditions proved to be efficient in the presence of functional diversity, yielding products in good to moderate yields. The release of molecular nitrogen as the only byproduct paves the way to an environmentally benign protocol. This method provides a single-step construction for amidated molecules, which are well established for their use in different ion detections and as WOLED molecules.

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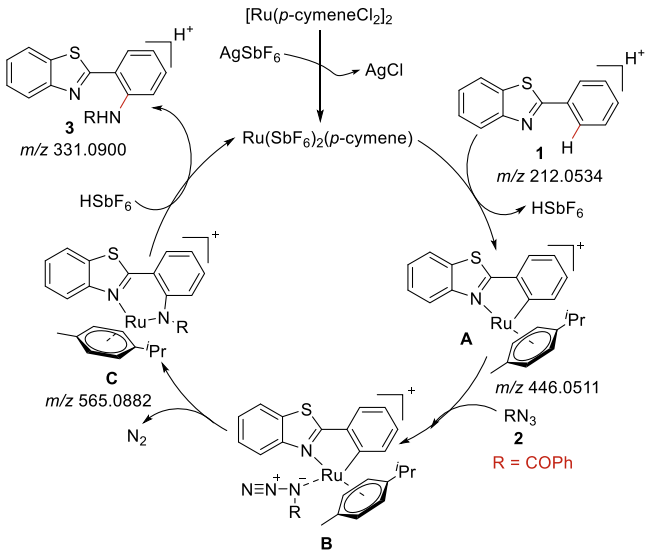
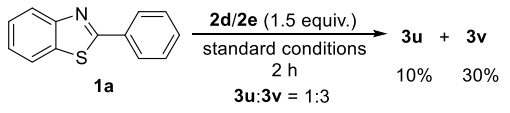
Scheme 2. Plausible Reaction Mechanism



Scheme 3. Intermolecular Competition Experiment: EDG vs EWG



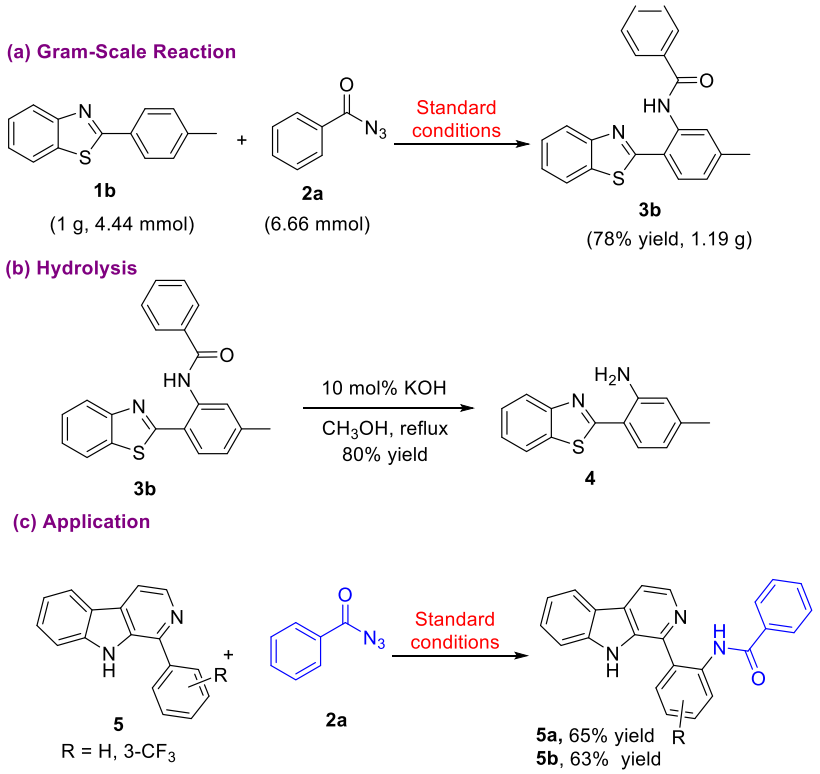
EXPERIMENTAL SECTION

General Information. Commercially available reagents and solvents were used without further purification. The ^{1}H NMR spectra were recorded on a NMR instrument operated at 500 MHz. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: δ = 7.25 ppm and DMSO-d_6: δ = 2.50 ppm). ^{13}C NMR spectra were recorded on a NMR instrument operated at 125 MHz with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: δ = 77.16 ppm and DMSO-d_6: δ = 39.52 ppm). The following abbreviations were used for ^{1}H NMR spectra to indicate the signal multiplicity: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), and dt (doublet of triplet). HRMS was measured in an ESI-MS mass spectrophotometer. Thin-layer chromatography was performed on MERCK precoated silica gel 60F-254 (0.5 mm) aluminum plates and visualized under UV light at 254 nm. Column chromatography was performed using silica gel 60−120 and 100−200 meshes.

Caution: The acyl azides are explosive in nature and hence should be stored below room temperature and the reactions should be handled carefully in sophisticated fume hoods. Precautions should be taken while using the rotary evaporator during the purification process wherein the temperature of the water bath should not exceed 30 °C.

General Procedure for Ru(II)-Catalyzed *Ortho*-Selective C−H Amidation of 2-Arylbenzothiazoles (3). 2-Arylbenzothiazoles **1** (1.0 equiv), benzoyl azides **2** (1.5 equiv), $[Ru(p\text{-cymene})Cl_2]_2$ (10 mol %), $AgSbF_6$ (20 mol %), and DCE (2 mL) were stirred at 80 °C for 5−7 h in a sealed tube. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with water and extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on a silica gel using 2−5% ethyl acetate in hexane as the eluent

Scheme 4. Gram-Scale, Hydrolysis Experiment, and Application



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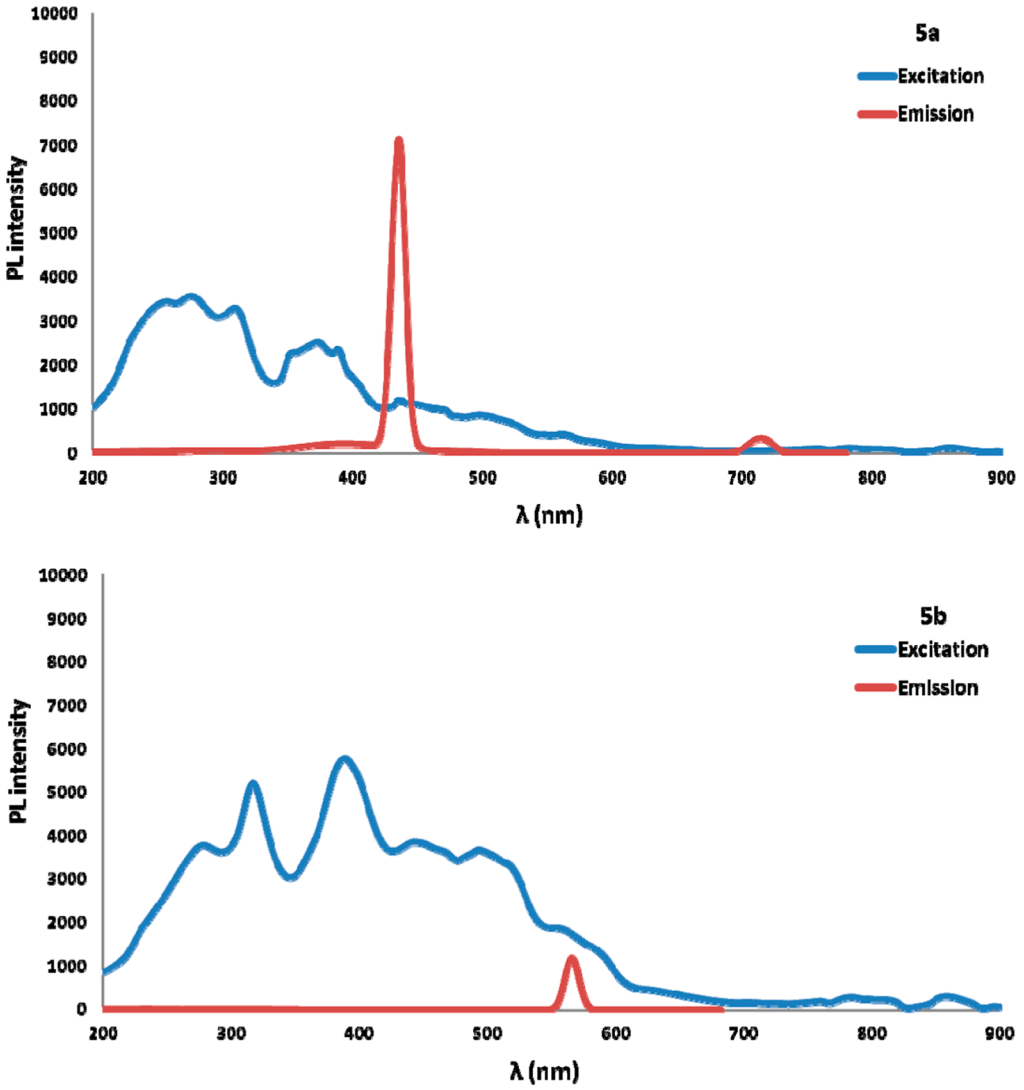

Figure 3. Absorption and emission spectra of **5a** and **5b**.

to give the desired product **3**. All the synthesized compounds were thoroughly characterized by IR, ^{1}H and ^{13}C NMR, and HRMS (ESI).

*N-(2-(Benzo[d]thiazol-2-yl)phenyl)benzamide (**3a**).* (76.3 mg), 70% yield, white solid, mp: 186−189 °C, FT-IR (cm)$^{-1}$: 3062, 1672, 1615, 1543, 1458; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.40 (s, 1H), 9.09 (d, J = 8.3 Hz, 1H), 8.27 (d, J = 5.6 Hz, 2H), 8.04 (d, J = 8.0 Hz, 1H), 7.96 (dd, J = 10.9, 8.0 Hz, 2H), 7.64 (d, J = 5.7 Hz, 3H), 7.58 (t, J = 7.6 Hz, 2H), 7.48 (t, J = 7.5 Hz, 1H), 7.24 (t, J = 7.5 Hz, 1H) ppm; ^{13}C{^{1}H} (125 MHz, $CDCl_3$): δ 169.1, 166.3, 152.8, 138.5, 135.7, 133.4, 132.2, 131.9, 129.9, 128.7, 127.8, 126.7, 125.9, 123.3, 122.3, 121.6, 120.9, 119.4 ppm; HRMS (ESI-QTOF): m/z [M + H]$^{+}$ calcd for $C_{20}H_{15}N_2OS$, 331.0900; found, 331.0899.

*N-(2-(Benzo[d]thiazol-2-yl)-5-methylphenyl)benzamide (**3b**).* (80.2 mg), 75% yield, white solid, mp: 162−165 °C, FT-IR (cm)$^{-1}$: 3023, 1691, 1615, 1598, 1511; ^{1}H NMR (500 MHz, DMSO-d_6): δ 13.07 (s, 1H), 8.70 (s, 1H), 8.21 (d, J = 7.6 Hz, 1H), 8.18−8.15 (m, 2H), 8.06 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.75−7.71 (m, 3H), 7.67−7.61 (m, 1H), 7.57−7.52 (m, 1H), 7.16 (dd, J = 8.0, 0.9 Hz, 1H), 2.44 (s, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6): δ 168.7, 165.7, 152.4, 142.9, 137.8, 134.8, 132.8, 132.6, 130.6, 129.2, 127.2, 126.7, 125.3, 122.7, 122.1, 121.7, 117.1, 21.5 ppm; HRMS (ESI-QTOF): m/z [M + H]$^{+}$ calcd for $C_{21}H_{17}N_2O_S$, 345.1056; found, 345.1050.

*N-(2-(Benzo[d]thiazol-2-yl)-5-isopropylphenyl)benzamide (**3c**).* (81.6 mg), 80% yield, white solid; mp: 180−183 °C; FT-IR (cm)$^{-1}$: 3089, 2961, 1671, 1618, 1578; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.38 (s, 1H), 8.99 (d, J = 1.6 Hz, 1H), 8.25 (m, 2H), 7.98 (d, J = 8.1 Hz, 1H), 7.92 (d, J = 7.6 Hz, 1H), 7.84 (d, J = 8.1 Hz, 1H), 7.63−7.57 (m, 3H), 7.56−7.49 (m, 1H), 7.45−7.39 (m, 1H), 7.08 (dd, J = 8.1, 1.6 Hz, 1H), 3.09−2.99 (m, 1H), 1.35 (s, 3H), 1.34 (s, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 169.1, 166.4, 153.8, 152.5, 138.9, 135.4, 133.0, 131.8, 129.9, 128.4, 128.0, 126.5, 125.7, 121.9, 121.3, 118.3, 117.0, 34.8, 23.7 ppm; HRMS (ESI-QTOF): m/z [M + H]$^{+}$ calcd for $C_{23}H_{21}N_2OS$, 373.1369; found, 373.1360.

*N-(2-(Benzo[d]thiazol-2-yl)-5-isopropoxyphenyl)-benzamide (**3d**).* (78.9 mg), 78% yield, white solid; mp: 184−187 °C; FT-IR (cm)$^{-1}$: 3062, 1671, 1625, 1583, 1413; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.52 (s, 1H), 8.74 (d, J = 2.5 Hz, 1H), 8.25 (dd, J = 7.5, 2.1 Hz, 2H), 7.92 (dd, J = 22.5, 7.8 Hz, 2H), 7.78 (d, J = 8.8 Hz, 1H), 7.65−7.58 (m, 3H), 7.55−7.48 (m, 1H), 7.43−7.35 (m, 1H), 6.71 (dd, J = 8.8, 2.6 Hz, 1H), 4.78 (dt, J = 12.1, 6.1 Hz, 1H), 1.43 (s, 3H), 1.42 (s, 3H) ppm;

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$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.9, 166.5, 161.2, 152.7, 140.3, 135.6, 133.0, 131.9, 131.3, 128.7, 127.9, 126.6, 125.3, 121.7, 121.4, 112.2, 105.9, 70.5, 22.0 ppm. HRMS (ESI-QTOF): m/z $[M + H]^+$ calcd for $C_{23}H_{20}N_2O_2S$, 389.1318; found, 389.1357.

*N-(2-(Benzo[d]thiazol-2-yl)-5-methoxyphenyl)benzamide (**3e**).* (80.5 mg), 77% yield, white solid, mp: 170−173 °C, FT-IR $(cm)^{-1}$: 3061, 2922, 1671, 1620, 1585; ^1H NMR (500 MHz, $CDCl_3$): δ 13.57 (s, 1H), 8.75 (d, J = 2.6 Hz, 1H), 8.25−8.24 (m, 2H), 7.91 (dd, J = 21.5, 7.8 Hz, 2H), 7.79 (d, J = 8.8 Hz, 1H), 7.64−7.60 (m, 3H), 7.51 (dd, J = 7.6, 6.6 Hz, 1H), 7.42−7.38 (m, 1H), 6.74 (dd, J = 8.8, 2.6 Hz, 1H), 3.95 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.0, 166.6, 162.8, 152.6, 140.3, 135.5, 132.9, 131.9, 131.1, 128.6, 127.8, 126.5, 125.4, 121.8, 121.4, 112.5, 110.9, 104.4, 55.6 ppm; HRMS (ESI-QTOF): m/z $[M + H]^+$ calcd for $C_{21}H_{17}N_2O_2S$, 361.1005; found, 361.1010.

*N-(2-(Benzo[d]thiazol-2-yl)-5-chlorophenyl)benzamide (**3f**).* (67.7 mg), 65% yield, white solid, mp: 148−150 °C, FT-IR $(cm)^{-1}$: 3112, 3055, 1673, 1620, 1580; ^1H NMR (500 MHz, $CDCl_3$): δ 13.40 (s, 1H), 9.10 (d, J = 2.0 Hz, 1H), 8.16 (d, J = 8.0 Hz, 2H), 7.94 (d, J = 8.1 Hz, 1H), 7.88 (d, J = 7.9 Hz, 1H), 7.76 (d, J = 8.5 Hz, 1H), 7.62−7.52 (m, 3H), 7.49 (t, J = 9.5 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.11 (dd, J = 8.4, 2.1 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.2, 152.4, 139.2, 138.3, 135.2, 132.1, 130.7, 128.7, 127.8, 127.0, 126.1, 123.4, 122.3, 121.6, 120.8, 117.8 ppm; HRMS (ESI-QTOF): m/z $[M + H]^+$ calcd for $C_{20}H_{14}ClN_2OS$, 365.0510; found, 365.0519.

*N-(2-(Benzo[d]thiazol-2-yl)-5-bromophenyl)benzamide (**3g**).* (62.2 mg), 63% yield, white solid, mp: 150−153 °C; FT-IR $(cm)^{-1}$: 2960, 1672, 1616, 1577, 698; ^1H NMR (500 MHz, $CDCl_3$): δ 13.44 (s, 1H), 9.32 (d, J = 2.0 Hz, 1H), 8.24−8.21 (m, 2H), 8.01 (d, J = 8.1 Hz, 1H), 7.96−7.93 (m, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.64−7.59 (m, 3H), 7.58−7.54 (m, 1H), 7.49−7.45 (m, 1H), 7.33 (dd, J = 8.4, 2.0 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.1, 165.9, 152.3, 139.1, 135.6, 132.8, 132.0, 130.6, 129.0, 128.4, 127.0, 126.7, 126.5, 126.1, 123.7, 122.3, 121.6, 118.1 ppm; HRMS (ESI-QTOF): m/z $[M + H]^+$ calcd for $C_{20}H_{14}BrN_2OS$, 409.0005; found, 409.0010.

*N-(2-(Benzo[d]thiazol-2-yl)-6-chlorophenyl)benzamide (**3h**).* (63.4 mg), 61% yield, white solid, mp: 144−147 °C, FT-IR $(cm)^{-1}$: 3112, 1687, 1612, 1589, 745; ^1H NMR (500 MHz, $CDCl_3$): δ 13.31 (s, 1H), 9.04 (d, J = 9.0 Hz, 1H), 8.21 (dd, J = 7.9, 1.7 Hz, 2H), 8.01 (d, J = 8.1 Hz, 1H), 7.95 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 2.4 Hz, 1H), 7.65−7.53 (m, 4H), 7.50−7.44 (m, 2H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.5, 166.2, 152.5, 137.0, 135.2, 133.3, 132.1, 131.9, 129.2, 128.7, 128.2, 127.8, 127.0, 126.3, 126.3, 122.5, 122.3, 121.7, 120.7 ppm; HRMS (ESI-QTOF): m/z $[M + H]^+$ calcd for $C_{20}H_{14}ClN_2OS$, 365.0510; found, 365.0513.

*N-(2-(Benzo[d]thiazol-2-yl)-3-fluorophenyl)benzamide (**3i**).* (66.6 mg), 64% yield, white solid; mp: 150−152 °C FT-IR $(cm)^{-1}$: 3020, 1679, 1660, 1593, 1314; ^1H NMR (500 MHz, DMSO-d_6): δ 13.68 (s, 1H), 8.77 (d, J = 8.4 Hz, 1H), 8.27 (d, J = 7.9 Hz, 1H), 8.15 (dd, J = 5.9, 2.5 Hz, 2H), 8.10 (d, J = 8.1 Hz, 1H), 7.73 (dd, J = 6.1, 2.7 Hz, 3H), 7.71−7.64 (m, 2H), 7.62−7.55 (m, 1H), 7.28 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6): δ 166.8, 161.8, 160.0, 150.2, 140.0, 135.2, 133.8, 133.6, 133.5, 132.9, 129.5, 127.8, 126.8, 122.7, 122.3, 117.0, 111.1, 111.0, 109.0, 108.9 ppm; HRMS (ESI-QTOF): m/z $[M + H]^+$ calcd for $C_{20}H_{13}FN_2OS$, 349.0805; found, 349.0799.

*N-(2-(Benzo[d]thiazol-2-yl)-5-(trifluoromethyl)phenyl)-benzamide (**3j**).* (72.8 mg), 73% yield, white solid, mp: 179−181 °C; FT-IR $(cm)^{-1}$: 3011, 1688, 1716, 1596, 1300; ^1H NMR (500 MHz, DMSO-d_6): δ 13.56 (s, 1H), 9.21 (d, J = 8.8 Hz, 1H), 8.25−8.21 (m, 2H), 8.12 (s, 1H), 8.00 (dd, J = 26.1, 8.0 Hz, 2H), 7.76 (d, J = 7.6 Hz, 1H), 7.67−7.56 (m, 4H), 7.49 (t, J = 7.5 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6): δ 162.9, 161.8, 147.8, 136.4, 130.3, 128.6, 127.6, 124.0, 123.1, 122.3, 122.0, 121.7, 117.7, 117.0, 116.3, 114.5 ppm; HRMS (ESI-QTOF): m/z $[M + H]^+$ calcd for $C_{21}H_{14}F_3N_2OS$, 399.0773; found, 399.0794.

*N-(2-(5,6-Dimethoxybenzo[d]thiazol-2-yl)phenyl)-benzamide (**3m**).* (79.5 mg), 79% yield, white solid, mp: 190−193 °C; FT-IR $(cm)^{-1}$: 3011, 2981, 1699, 1578, 1500; ^1H NMR (500 MHz, $CDCl_3$): δ 13.39 (s, 1H), 9.03 (d, J = 8.4 Hz, 1H), 8.25−8.23 (m, 2H), 7.84 (dd, J = 7.9, 1.3 Hz, 1H), 7.61−7.55 (m, 3H), 7.53−7.48 (m, 1H), 7.45 (s, 1H), 7.33 (s, 1H), 7.20−7.16 (m, 1H), 4.02 (s, 3H), 4.00 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.2, 166.3, 149.8, 149.3, 147.0, 138.0, 135.9, 131.8, 131.5, 129.3, 128.5, 127.9, 125.7, 123.3, 120.8, 119.8, 119.75, 111.4, 103.8, 102.4, 56.4, 56.1 ppm; HRMS (ESI-QTOF): m/z $[M + H]^+$ calcd for $C_{22}H_{19}N_2O_3S$, 391.1111; found, 391.1158.

*N-(2-(5-Methylbenzo[d]thiazol-2-yl)phenyl)benzamide (**3n**).* (80.6 mg), 75% yield, white solid, mp: 168−171 °C: FT-IR $(cm)^{-1}$: 3016, 1699, 1612, 1577, 1485; ^1H NMR (500 MHz, $CDCl_3$): δ 13.40 (s, 1H), 9.05 (dd, J = 8.5, 1.0 Hz, 1H), 8.25−8.22 (m, 2H), 7.91−7.86 (m, 2H), 7.73 (s, 1H), 7.62−7.58 (m, 3H), 7.55−7.51 (m, 1H), 7.35 (dd, J = 8.3, 1.2 Hz, 1H), 7.20 (m, 1H), 2.52 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 163.2, 161.5, 146.1, 133.6, 131.4, 130.9, 128.8, 127.2, 127.1, 125.0, 123.9, 123.5, 123.1, 118.5, 117.0, 116.5, 116.1, 114.8, 16.9 ppm; HRMS (ESI-QTOF): m/z $[M + H]^+$ calcd for $C_{21}H_{17}N_2OS$, 345.1056; found, 345.1085.

*N-(2-(Benzo[d]thiazol-2-yl)phenyl)-3-methoxybenzamide (**3p**).* (87.2 mg), 73% yield, white solid, mp: 160−163 °C; FT-IR $(cm)^{-1}$: 3169, 3001, 1669, 1613, 1538, 1487; ^1H NMR (500 MHz, DMSO-d_6): δ 13.03 (s, 1H), 8.81 (d, J = 8.4 Hz, 1H), 8.23 (d, J = 8.0 Hz, 1H), 8.10−8.05 (m, 2H), 7.76 (d, J = 7.7 Hz, 1H), 7.68−7.62 (m, 4H), 7.55 (m, 1H), 7.36−7.32 (m, 1H), 7.30 (dd, J = 8.2, 2.6 Hz, 1H), 3.90 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6): δ 168.7, 165.5, 160.1, 152.5, 137.9, 136.6, 133.4, 132.7, 130.7, 130.7, 127.7, 126.7, 124.6, 122.8, 122.5, 121.1, 120.1, 119.7, 117.9, 113.8, 55.9 ppm; HRMS (ESI-QTOF): m/z $[M + H]^+$ calcd for $C_{21}H_{17}N_2O_2S$, 361.1005; found, 361.1006.

*N-(2-(Benzo[d]thiazol-2-yl)-5-methoxyphenyl)-3-methoxybenzamide (**3q**).* (80.4 mg), 71% yield, white solid; mp: 182−185 °C; FT-IR $(cm)^{-1}$: 2965, 2838, 1678, 1625, 1544; ^1H NMR (500 MHz, $CDCl_3$): δ 13.57 (s, 1H), 8.74 (d, J = 2.6 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.86 (ddd, J = 4.7, 2.3, 0.6 Hz, 2H), 7.80−7.78 (m, 2H), 7.54−7.49 (m, 2H), 7.40 (dd, J = 8.0, 1.0 Hz, 1H), 7.15 (m, 1H), 6.74 (dd, J = 8.8, 2.6 Hz, 1H), 3.95 (s, 3H), 3.93 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.0, 166.4, 162.7, 160.1, 152.8, 140.3, 137.0, 132.9, 131.2, 129.6, 126.6, 125.4, 121.9, 121.4, 119.8, 117.8, 113.5, 112.6, 111.0, 104.4, 55.5 ppm; HRMS (ESI-QTOF): m/z $[M + H]^+$ calcd for $C_{22}H_{19}N_2O_3S$, 391.1111; found, 391.1112.

*N-(2-(Benzo[d]thiazol-2-yl)-5-isopropylphenyl)-3-methoxybenzamide (**3r**).* (86.7 mg), 78% yield, white solid, mp: 160−

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163 °C; FT-IR (cm)$^{-1}$: 3003, 2960, 2836, 1681, 1618; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.37 (s, 1H), 8.98 (d, J = 1.6 Hz, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.91 (d, J = 7.7 Hz, 1H), 7.84 (dd, J = 8.1, 5.4 Hz, 2H), 7.82−7.77 (m, 1H), 7.56−7.48 (m, 2H), 7.46−7.38 (m, 1H), 7.15 (m, 1H), 7.08 (dd, J = 8.1, 1.6 Hz, 1H), 3.93 (s, 3H), 3.03 (m, 1H), 1.35 (s, 3H), 1.34 (s, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 169.0, 166.2, 160.0, 154.2, 152.6, 138.4, 136.9, 133.0, 129.6, 129.6, 126.6, 125.6, 122.3, 121.6, 121.5, 119.7, 118.9, 117.2, 117.2, 113.5, 55.7, 34.5, 23.7 ppm; HRMS (ESI-QTOF): m/z [M + H]$^+$ calcd for $C_{24}H_{23}N_2O_2S$, 403.1475; found, 403.1474.

*N-(2-(Benzo[d]thiazol-2-yl)-5-chlorophenyl)-3-methoxybenzamide (**3s**).* (73.1 mg), 65% yield, white solid, mp: 180−182 °C; FT-IR (cm)$^{-1}$: 2960, 2831, 1682, 1618, 1581; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.44 (s, 1H), 9.14 (d, J = 1.9 Hz, 1H), 8.05 (d, J = 8.1 Hz, 1H), 7.92 (d, J = 7.9 Hz, 1H), 7.80 (dd, J = 7.9, 3.0 Hz, 2H), 7.77 (s, 1H), 7.53 (dt, J = 14.3, 7.9 Hz, 2H), 7.45 (t, J = 7.6 Hz, 1H), 7.16 (d, J = 8.4 Hz, 2H), 3.93 (s, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 168.0, 166.2, 160.2, 152.4, 139.2, 138.2, 136.6, 133.1, 130.7, 129.7, 126.9, 126.1, 123.4, 122.5, 121.5, 120.7, 119.7, 117.8, 117.7, 113.7, 55.5 ppm; HRMS (ESI-QTOF): m/z [M + H]$^+$ calcd for $C_{21}H_{16}ClN_2O_2S$, 395.0616; found, 395.0623.

*N-(2-(Benzo[d]thiazol-2-yl)phenyl)-4-methylbenzamide (**3t**).* (91.7 mg), 80% yield, white solid, mp: 198−201 °C; FT-IR (cm)$^{-1}$: 3021, 1689, 1614, 1578, 1512; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.21 (s, 1H), 8.99 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 8.2 Hz, 2H), 7.95 (d, J = 8.1 Hz, 1H), 7.90−7.80 (m, 2H), 7.55−7.42 (m, 2H), 7.39 (dd, J = 11.6, 4.6 Hz, 1H), 7.33 (d, J = 8.0 Hz, 2H), 7.13 (dd, J = 11.6, 4.7 Hz, 1H), 2.42 (s, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 168.2, 165.2, 151.7, 141.2, 137.5, 132.4, 131.7, 131.2, 128.9, 128.3, 126.9, 125.7, 124.8, 122.1, 121.3, 120.6, 119.9, 118.3, 20.3 ppm; HRMS (ESI-QTOF): m/z [M + H]$^+$ calcd for $C_{21}H_{17}N_2OS$, 345.1056; found, 345.1052.

*N-(2-(Benzo[d]thiazol-2-yl)phenyl)-3,4,5-trimethoxybenzamide (**3u**).* (109.0 mg), 78% yield, white solid, mp: 140−144 °C; FT-IR (cm)$^{-1}$: 3096, 2945, 1687, 1612, 1566; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.18 (s, 1H), 8.99 (d, J = 8.4 Hz, 1H), 8.09−7.75 (m, 3H), 7.58−7.49 (m, 2H), 7.47−7.41 (m, 1H), 7.39 (s, 2H), 7.22 (m, 1H), 3.98 (s, 3H), 3.96 (s, 6H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 169.1, 166.4, 153.4, 152.8, 138.4, 133.3, 132.2, 131.5, 130.0, 126.7, 125.9, 123.3, 122.3, 121.6, 120.8, 119.4, 106.1, 61.0, 56.8 ppm; HRMS (ESI-QTOF): m/z [M + H]$^+$ calcd for $C_{23}H_{21}N_2O_4S$, 421.1217; found, 421.1262.

*N-(2-(Benzo[d]thiazol-2-yl)phenyl)-4-nitrobenzamide (**3v**).* (86.8 mg) 70% yield, yellow solid, mp: 170−172 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.61 (s, 1H), 9.01 (d, J = 8.3 Hz, 1H), 8.43 (dd, J = 30.4, 8.6 Hz, 4H), 7.96 (t, J = 7.9 Hz, 3H), 7.63−7.55 (m, 2H), 7.49 (t, J = 7.6 Hz, 1H), 7.28 (s, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 169.1, 164.0, 152.5, 141.2, 137.8, 133.2, 132.4, 130.0, 128.9, 127.1, 126.2, 124.1, 123.9, 122.1, 121.8, 120.9, 119.6 ppm; HRMS (ESI-QTOF): m/z [M + H]$^+$ calcd for $C_{20}H_{14}N_3O_3S$, 376.0750; found, 376.0756.

*N-(2-(Benzo[d]thiazol-2-yl)phenyl)-3-iodobenzamide (**3w**).* (106.3 mg), 70% yield, white solid, mp: 160−163 °C; FT-IR (cm)$^{-1}$: 3058, 1675, 1612, 1588, 1489; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.35 (s, 1H), 9.02 (dd, J = 8.5, 0.9 Hz, 1H), 8.54 (t, J = 1.6 Hz, 1H), 8.23 (d, J = 8.1 Hz, 1H), 8.19 (dd, J = 8.0, 1.3 Hz, 1H), 7.99−7.88 (m, 3H), 7.60−7.51 (m, 2H), 7.46 (m, 1H), 7.34 (t, J = 7.8 Hz, 1H), 7.22 (m, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 169.0, 164.5, 152.7, 140.8, 138.0, 137.5, 136.3, 133.2, 132.2, 130.4, 129.8, 127.4, 126.8, 126.0, 123.6, 123.0, 121.5, 120.9, 119.5, 94.3 ppm; HRMS (ESI-QTOF): m/z [M + H]$^+$ calcd for $C_{20}H_{14}IN_2OS$, 456.9866; found, 456.9867.

*N-(2-(Benzo[d]thiazol-2-yl)-5-isopropylphenyl)-4-iodobenzamide (**3x**).* (99.5 mg), 72% yield, white solid, mp: 180−183 °C; FT-IR (cm)$^{-1}$: 2959, 2868, 1672.40, 1617, 1578; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.36 (s, 1H), 8.95 (d, J = 1.5 Hz, 1H), 8.56 (t, J = 1.6 Hz, 1H), 8.21 (dd, J = 11.0, 4.5 Hz, 2H), 7.94 (t, J = 8.5 Hz, 2H), 7.85 (d, J = 8.1 Hz, 1H), 7.58−7.50 (m, 1H), 7.47−7.41 (m, 1H), 7.34 (t, J = 7.8 Hz, 1H), 7.10 (dd, J = 8.1, 1.6 Hz, 1H), 3.04 (m, 1H), 1.35 (s, 3H), 1.34 (s, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 169.0, 164.6, 154.0, 152.6, 140.6, 138.1, 137.4, 136.2, 133.1, 130.5, 130.0, 127.4, 126.7, 125.8, 122.8, 121.9, 121.5, 119.0, 117.4, 94.3, 34.5, 23.7 ppm; HRMS (ESI-QTOF): m/z [M + H]$^+$ calcd for $C_{23}H_{20}IN_2OS$, 499.0336; found, 499.0335.

*N-(2-(Benzo[d]thiazol-2-yl)-6-chlorophenyl)-4-iodobenzamide (**3y**).* (95.5 mg), 68% yield, white solid, mp: 178−180 °C; FT-IR (cm)$^{-1}$: 3011, 2977, 1691, 1655, 1596; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.28 (s, 1H), 9.00 (d, J = 9.0 Hz, 1H), 8.51 (t, J = 1.6 Hz, 1H), 8.25 (d, J = 8.1 Hz, 1H), 8.18−8.15 (m, 1H), 7.97−7.93 (m, 2H), 7.86 (d, J = 2.4 Hz, 1H), 7.61−7.55 (m, 1H), 7.52−7.46 (m, 2H), 7.33 (t, J = 7.8 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 167.3, 164.5, 152.6, 140.9, 137.2, 136.7, 136.2, 133.2, 131.9, 130.5, 129.2, 128.5, 127.4, 127.0, 126.4, 123.2, 122.4, 121.6, 120.8, 94.3 ppm; HRMS (ESI-QTOF): m/z [M + H]$^+$ calcd for $C_{20}H_{13}ClIN_2OS$, 490.9476; found, 490.9480.

*N-(2-(Benzo[d]thiazol-2-yl)phenyl)-3,5-dichlorobenzamide (**3z**).* (79.2 mg), 60% yield, white solid, mp: 210−213 °C; FT-IR (cm)$^{-1}$: 3071, 2917, 1677, 1620.74, 1547; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.46 (s, 1H), 9.00 (d, J = 8.1 Hz, 1H), 8.23 (d, J = 7.8 Hz, 1H), 8.15 (s, 2H), 8.00−7.88 (m, 2H), 7.57 (dd, J = 20.4, 11.6 Hz, 3H), 7.47 (t, J = 7.2 Hz, 1H), 7.23 (d, J = 7.5 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 168.6, 163.4, 152.8, 138.3, 137.8, 135.6, 135.1, 133.2, 132.3, 131.7, 129.9, 126.9, 126.4, 126.1, 123.9, 122.6, 121.5, 120.9, 119.5 ppm; HRMS (ESI-QTOF): m/z [M + H]$^+$ calcd for $C_{20}H_{12}Cl_2N_2OS$, 399.0120; found, 399.0121.

*N-(2-(Benzo[d]thiazol-2-yl)-5-methylphenyl)-3,5-dichlorobenzamide (**3ab**).* (83.6 mg), 65% yield, white solid, mp: 170−174 °C, FT-IR (cm)$^{-1}$: 2914, 1678, 1623, 1591, 1566; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.40 (s, 1H), 8.83 (s, 1H), 8.20 (d, J = 8.0 Hz, 1H), 8.14 (s, 2H), 7.92 (d, J = 7.8 Hz, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.59 (s, 1H), 7.55 (t, J = 7.6 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 7.04 (d, J = 7.9 Hz, 1H), 2.47 (s, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 169.1, 163.5, 153.0, 143.4, 138.7, 137.9, 135.7, 133.1, 131.4, 130.2, 126.8, 126.4, 125.8, 124.8, 122.4, 121.4, 121.2, 117.1, 22.0 ppm; HRMS (ESI-QTOF): m/z [M + H]$^+$ calcd for $C_{21}H_{15}Cl_2N_2OS$, 413.0277; found, 413.0279.

*N-(2-(Benzo[d]thiazol-2-yl)-5-isopropylphenyl)-3,5-dichlorobenzamide (**3ac**).* (81.8 mg), 67% yield, white solid, mp: 170−173 °C; FT-IR (cm)$^{-1}$: 3081, 2965, 1679, 1619, 1577; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.43 (s, 1H), 8.92 (d, J = 1.7 Hz, 1H), 8.20 (d, J = 8.1 Hz, 1H), 8.15 (d, J = 1.9 Hz, 2H), 7.91 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 8.1 Hz, 1H), 7.59 (t, J = 1.9 Hz, 1H), 7.57−7.51 (m, 1H), 7.46−7.41 (m, 1H), 7.10 (m, 1H), 3.04 (m, 1H), 1.35 (s, 3H), 1.34 (s, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 168.9, 163.2, 153.8, 152.3, 138.1, 138.0, 135.2, 132.8, 131.7, 129.9, 126.8, 126.8,

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125.8, 122.5, 122.1, 121.4, 118.9, 117.4, 34.6, 23.6 ppm; HRMS (ESI-QTOF): m/z [M + H]$^+$ calcd for $C_{23}H_{18}Cl_2N_2OS$, 441.0590; found, 441.0592.

*N-(2-(Benzo[d]thiazol-2-yl)-5-isopropoxyphenyl)-3,5-dichlorobenzamide (**3ad**).* (78.5 mg), 66% yield, white solid, mp: 169−172 °C; FT-IR (cm)$^{-1}$: 2978, 1682, 1625, 1583, 1478; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.53 (s, 1H), 8.63 (d, J = 2.4 Hz, 1H), 8.14 (s, 1H), 8.12 (d, J = 1.7 Hz, 2H), 7.86 (d, J = 7.9 Hz, 1H), 7.75 (d, J = 8.8 Hz, 1H), 7.57 (s, 1H), 7.50 (t, J = 7.4 Hz, 1H), 7.38 (t, J = 7.4 Hz, 1H), 6.70 (dd, J = 8.8, 2.5 Hz, 1H), 4.74 (m, 1H), 1.43 (s, 3H), 1.42 (s, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 169.0, 163.4, 161.1, 152.6, 139.5, 138.2, 135.6, 132.7, 131.6, 131.3, 126.7, 126.4, 125.4, 122.1, 121.3, 112.4, 112.2, 106.1, 70.4, 29.7, 22.0 ppm; HRMS (ESI-QTOF): m/z [M + H]$^+$ calcd for $C_{23}H_{19}Cl_2N_2O_2S$, 457.0539; found, 457.0533.

*N-(2-(Benzo[d]thiazol-2-yl)phenyl)cinnamamide (**3ae**).* (70.0 mg), 60% yield, white solid, mp: 190−193 °C; FT-IR (cm)$^{-1}$: 2986, 2563, 1675, 1586, 998; ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.76 (s, 1H), 8.90 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 8.1 Hz, 1H), 7.88 (d, J = 7.9 Hz, 1H), 7.83 (d, J = 8.8 Hz, 1H), 7.75 (d, J = 15.7 Hz, 1H), 7.57 (d, J = 7.0 Hz, 2H), 7.50 (t, J = 7.7 Hz, 1H), 7.45 (t, J = 7.3 Hz, 1H), 7.42−7.32 (m, 4H), 7.12 (t, J = 7.6 Hz, 1H), 6.68 (d, J = 15.7 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 168.9, 165.0, 153.0, 141.6, 138.2, 135.1, 132.2, 130.0, 129.0, 128.0, 126.7, 125.9, 123.3, 122.8, 122.6, 121.6, 121.0, 119.2 ppm; HRMS (ESI-QTOF): m/z [M + H]$^+$ calcd for $C_{22}H_{17}N_2OS$, 357.1056; found, 357.1050.

Competition Experiment Using Acyl Azides 2d and 2e. 2-Phenyl benzthiazole **1a** (1 equiv), **2d** (1.5 equiv), **2e** (1.5 equiv), [Ru(p-cymene)Cl$_2$]$_2$ (10 mol %), and AgSbF$_6$ (20 mol %) in DCE (2.0 mL) were subjected to the standard reaction conditions described in the general procedure for 2 h to produce **3u** and **3v** in 10 and 30% yields, respectively.

Gram-Scale Reaction. To demonstrate the scalability of the regioselective amidation, a gram-scale synthesis was performed using **1b** (1.5 g, 4.44 mmol) and **2a** (6.66 mmol) under the optimized conditions, as discussed in the general procedure. The reaction proceeded efficiently to give the desired product **3b** (1.19 g) in 78% yield.

General Procedure for Hydrolysis of *N*-(2-(Benzo[*d*]-thiazol-2-yl)-5-methylphenyl)benzamide (4). *N*-(2-(Benzo[*d*]thiazol-2-yl)-5-methylphenyl)benzamide **3b** (0.2 mmol) was refluxed in methanol in the presence of 10 mol % KOH. After completion of the reaction (monitored by TLC), the residual solvent was removed under reduced pressure. Further reaction mixture was extracted using ethyl acetate and water. The combined organic layers were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on a silica gel using 20% ethyl acetate in hexane as the eluent to give the desired 2-(benzo[d]thiazol-2-yl)methylaniline (**4**) (39 mg), 80% yield, white solid, mp: 210−220 °C; FT-IR (cm)$^{-1}$: 3400, 3320, 1677, 1578, 1300; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.07 (d, J = 7.9 Hz, 1H), 7.98 (d, J = 8.1 Hz, 1H), 7.51 (dd, J = 17.5, 7.7 Hz, 2H), 7.41 (t, J = 7.6 Hz, 1H), 7.28 (s, 2H), 6.70 (s, 1H), 6.50 (d, J = 8.0 Hz, 1H), 2.24 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 169.3, 153.8, 148.1, 142.2, 132.7, 130.4, 126.8, 125.4, 122.3, 122.1, 117.6, 116.9, 111.5, 21.7 ppm; HRMS (ESI-QTOF): m/z [M + H]$^+$ calcd for $C_{14}H_{12}N_2S$, 241.0794; found, 241.0794.

General Procedure for *ortho*-Amidation of 2-Phenyl-Substituted β-Carbolines (5a and b). The 2-phenyl-substituted β-carbolines[24a] **5** (1 equiv), benzoyl azides **2** (1.5 equiv), [Ru(p-cymene)Cl$_2$]$_2$ (10 mol %), AgSbF$_6$ (20 mol %), and DCE (2 mL) were stirred at 80 °C for 12 h in a sealed tube. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with water and extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on a silica gel using 20% ethyl acetate in hexane as the eluent to give the desired product **5a** and **5b**.

*N-(2-(9H-Pyrido[3,4-b]indol-1-yl)phenyl)benzamide (**5a**).* (67.68 mg), 65% yield white solid, mp: 222−225 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.47 (s, 1H), 11.67 (s, 1H), 8.61 (d, J = 5.2 Hz, 1H), 8.57 (d, J = 8.2 Hz, 1H), 8.31 (d, J = 7.9 Hz, 1H), 8.26 (d, J = 5.2 Hz, 1H), 8.05 (dd, J = 7.7, 1.4 Hz, 1H), 7.90−7.86 (m, 2H), 7.67 (d, J = 8.2 Hz, 1H), 7.61−7.54 (m, 5H), 7.44 (td, J = 7.5, 1.2 Hz, 1H), 7.30 (t, J = 7.2 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.6, 141.8, 141.7, 137.4, 137.1, 135.0, 134.0, 132.4, 130.7, 130.2, 129.8, 129.4, 129.3, 129.1, 127.3, 126.47, 124.7, 122.4, 122.3, 122.2, 121.2, 120.3, 118.6, 115.1, 113.0 ppm; HRMS (ESI-QTOF): m/z [M + H]$^+$ calcd for $C_{24}H_{18}N_3O$, 364.1444; found, 364.1457.

*N-(2-(9H-Pyrido[3,4-b]indol-1-yl)-3-(trifluoromethyl)-phenyl)benzamide (**5b**).* (60.92 mg), 63% yield, white solid mp: 226−229 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.34 (s, 1H), 11.83 (s, 1H), 8.76 (d, J = 8.6 Hz, 1H), 8.63 (d, J = 5.2 Hz, 1H), 8.32 (dd, J = 12.4, 6.5 Hz, 2H), 8.26 (s, 1H), 7.95 (d, J = 8.5 Hz, 1H), 7.86 (d, J = 7.2 Hz, 2H), 7.68−7.53 (m, 5H), 7.31 (t, J = 7.4 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.04, 141.85, 140.47, 140.24, 137.67, 134.56, 132.7, 131.1, 129.4, 129.3, 127.5, 127.1, 127.0, 122.9, 122.4, 121.3, 120.4, 115.7, 112.9 ppm; HRMS (ESI-QTOF): m/z [M + H]$^+$ calcd for $C_{25}H_{17}N_3F_3O$, 432.1318; found, 432.1323.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.1c05910.

Copies of ^{1}H and ^{13}C{^{1}H} NMR spectra for the isolated final products **3a−3ae**, **4**, **5a**, and **5b** (PDF)

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Notes

The authors declare no competing financial interest.

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