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To be cited as: *Adv. Synth. Catal.* 10.1002/adsc.202001149

Link to VoR: https://doi.org/10.1002/adsc.202001149

10.1002/adsc.202001149

FULL PAPER

DOI: 10.1002/adsc.201((will be filled in by the editorial staff))

P(III)-Mediated Cascade C-N/C-S Bond Formation: An Protocol towards the Synthesis of *N,S*-Heterocycles and Spiro Compounds

Saibabu Polina,[a] V. P. Rama Kishore Putta,[a] Raghuram Gujjarappa,[b] Virender Singh,[c] Prasad Pralhad Pujar,[a]* and Chandi C. Malakar[b]*

[a] Department of Chemistry, CHRIST (Deemed to be University), Bangalore - 560029, India
Phone: 080-40129313, Fax: +91 8040129000, Email: prasad.pujar@christuniversity.in
[b] Department of Chemistry, National Institute of Technology Manipur, Langol, Imphal - 795004, Manipur, India
Phone: (+91) 0385-2058566, Fax: (+91) 0385-2445812, Email: chdeepm@gmail.com; cmalakar@nitmanipur.ac.in
[c] Department of Chemistry, Central University of Punjab, Bathinda, 151001, Punjab, India

Received: ((will be filled in by the editorial staff))

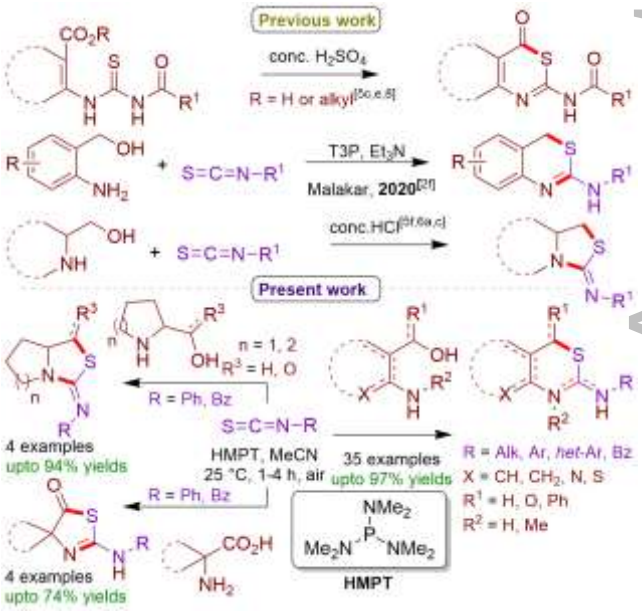
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201######.((Please delete if not appropriate))

Abstract. A P(III)-mediated entry towards construction of C-N/C-S bond has been devised. The developed heterocyclization method was exercised for the synthesis of a diverse range of *N,S*-heterocycles and related spiro molecules. $P(NMe_2)_3$ revealed the maximum efficacies under the aerobic reaction conditions and a spectrum of bis-nucleophiles, and isothiocyanates were tolerated well to serve the access of manifold immense molecules.

Keywords: Benzothiazin-4-ones; Cascade reaction; *N,S*-heterocycles; $P(NMe_2)_3$; Spiro compounds

Introduction

Nitrogen and sulphur containing heterocycles play an impeccable and irreplaceable role in the field of medicinal chemistry owing to their unique pharmacological properties.[1-7] In particular, heterocyclic moieties such as benzothiazinones, benzothiazines, pyrrolo[1,2-*c*]thiazoles and 3-thia-1-azaspiro cores are well-recognized for their broad spectrum of biological properties.[1,3-7] Benzothiazinones are eminently explored for their *in vitro* inhibition of monoacylglycerol lipase (MGL) activity,[5b] antagonizing adenosine receptors (A_{2A} ARs) and inhibiting monoamine oxidase B (MAO-B).[5c,e] Albeit, these scaffolds possess vital pharmacological properties, their synthetic strategies have been rarely investigated. The synthesis of benzothiazinones are largely accomplished by the cyclization of aroylthioureas in presence of conc. H_2SO_4.[5c,e,8] Our research group has recently reported the synthesis of benzothiazines by employing T3P (2,4,6-tripropyl-1,3,5,2,4,6-trioxatriphosphorinane-2,4,6-trioxide)-mediated cyclization of 2-amino-arylalkyl alcohols with isothiocyanates.[2f] Afar from these protocols, several other useful approaches towards the preparation of benzothiazine motifs are known.[3e,9] Likewise, the synthesis of pyrrolo[1,2-*c*]thiazoles was realized by the cyclization of prolinol derivatives with isothiocyanates in presence of conc. HCl.[5f,6a,c] In contrast, structurally enthralling 3-thia-1-azaspiro compounds are barely explored, albeit their medicinal importance.[7] In continuation of our research in this area,[2f] here we have reported $P(NMe_2)_3$-mediated annulation reactions of bis-nucleophiles and isothiocyanates towards the preparation of diversified *N,S*-heterocycles (Scheme 1).



Scheme 1. Approaches towards the synthesis of various *N,S*-heterocycles.

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Results and Discussion

We initiated our experiments by considering anthranilic acid (**1a**) and benzoyl isothiocyanate (**2a**) as model substrates. At the onset, we have screened various organophosphine (PR_3) reagents such as trimethyl phosphite ($P(OMe)_3$), dimethylphosphine ($PHMe_2$), tributylphosphine (P^nBu_3), trimethylphosphine (PMe_3), triphenylphosphine (PPh_3), 2,4,6-tripropyl-1,3,5,2,4,6-trioxatriphosphorinane-2,4,6-trioxide (T3P), hexamethylphosphoramide (HMPA) and hexamethylphosphorous triamide (HMPT) towards the formation of the product benzothiazinone **4aa** (entries 1-8).

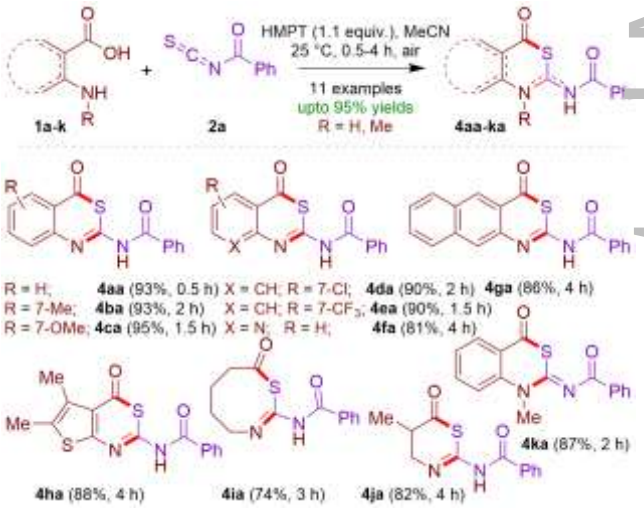
Table 1. Optimization of reaction conditions.[a)]

Entry	Reaction conditions	%Yield **4aa**[b)] (% conv.)[c)]
1	$P(OMe)_3$ (2 equiv.), Et_3N (2.2 equiv.), MeCN, 8 h	0 (trace)
2	$PHMe_2$ (2 equiv.), Et_3N (2.2 equiv.), MeCN, 8 h	0 (trace)
3	P^nBu_3 (2 equiv.), Et_3N (2.2 equiv.), MeCN, 8 h	0 (<20)
4	PMe_3 (2 equiv.), Et_3N (2.2 equiv.), MeCN, 8 h	0 (<15)
5	PPh_3 (2 equiv.), Et_3N (2.2 equiv.), THF, 6 h	0 (trace)
6	T3P (1.1 equiv.), Et_3N (2.2 equiv.), MeCN, 8 h	67 (80)
7	HMPA (1.1 equiv.), Et_3N (2.2 equiv.), PhMe, 16 h	0 (<20)
8	HMPT (1.1 equiv.), Et_3N (2.2 equiv.), PhMe, 4 h	83 (91)
9	HMPT (1.1 equiv.), Et_3N (1.1 equiv.), PhMe, 4 h	83 (94)
10	HMPT (1.1 equiv.), PhMe, 4 h	86 (98)
11	HMPT (1.1 equiv.), EtOAc, 6 h	55 (72)
12	HMPT (1.1 equiv.), CH_2Cl_2, 6 h	46 (63)
13	HMPT (1.1 equiv.), DMSO, 6 h	31 (47)
14	HMPT (1.1 equiv.), DMF, 3 h	40 (60)
15	**HMPT (1.1 equiv.), MeCN, 0.5 h**	**93 (100)**
16	HMPT (1.1 equiv.), THF, 3 h	85 (95)
17	HMPT (0.75 equiv.), MeCN, 0.5 h	74 (90)
18	HMPT (0.50 equiv.), MeCN, 0.5 h	52 (70)

[a)] All reactions were performed using 1.0 mmol **1a** and 1.1 mmol **2a** in 2 mL of solvent at 25 °C under air. [b)] Isolated yields. [c)] Conversion was monitored by LC−MS

To our dismay, most of the screened reagents were inactive for the formation of desired product **4aa**, rather the reaction was terminated at the intermediate **3aa** stage. Surprisingly, among the screened phosphine reagents, the $P(NMe_2)_3$ (HMPT, Hexamethylphosphorous triamide) showed greater efficacy in terms of conversion (91%) and yield (83%). Notably, the reaction conditions were found competent even with reduced amounts of base and also in absence of base to obtain product **4aa** in similar yields of 83% and 86% respectively (entries 9-10). Upon screening of solvents (entries 11-16), it was found that MeCN facilitates the formation of product **4aa** in higher yield of 93% (entry 15). However, when the reaction was performed using reduced amounts of HMPT, the unsuccessful results were obtained (entries 17-18).

After screening the reaction conditions, we have examined the scope of different 2-aminoaryl carboxylic acids **1a-h** with benzoyl isothiocyanate (**2a**) to obtain diverse range of benzothiazinones **4aa-4ha** in yields up to 95% (Scheme 2). The developed reaction conditions proved to be efficient for the preparation of thiazinone derivatives **4ia-ka** in good to excellent yields with high functional group tolerance.



Scheme 2. Scope of thiazinones.

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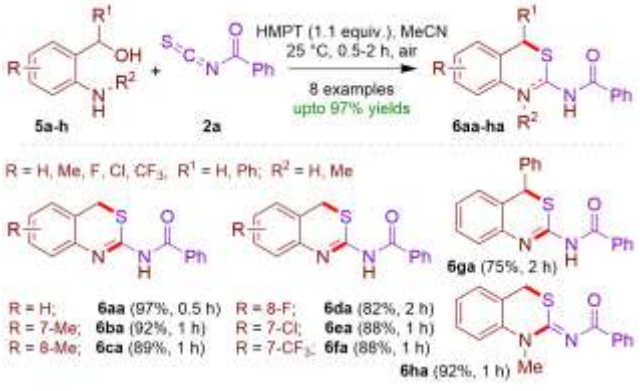
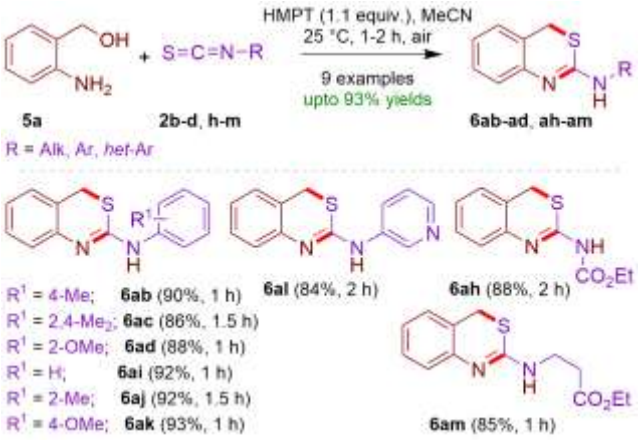
Scheme 3. Scope of different isothiocyanates **2**.

Thereafter, we focused on elaborating the scope of the reaction conditions with differently substituted isothiocyanates **2d-h** (Scheme 3). The aromatic isothiocyanates with electron rich (methyl, methoxy) as well as electron poor (F, CF_3) functional groups performed well under optimal reaction conditions by delivering the products **4ab-ag** in excellent yields. Alkyl isothiocyanate **2h** also reacted in a desired pattern to produce **4ah** in 88% yield.

Further, in order to expand the scope of the developed methodology, variety of 2-aminobenzyl alcohols **5a-h** were investigated for reaction with benzoyl isothiocyanate (**2a**). As a result, we have obtained the corresponding benzothiazine derivatives **6aa-ha** in the range of 88-97% yields (Scheme 4). Moreover, 2-aminobenzyl alcohol (**5a**) was treated with aryl/alkyl isothiocyanates **2b-d**, **h**, **j-m** accommodated with various functional groups to afford the corresponding benzothiazines **6ab-ad**, **ah-am** in excellent yields (Scheme 5).



Scheme 4. Scope of 2-aminobenzyl alcohols **5a-h**.



Scheme 5. Scope of isothiocyanates **2** towards the synthesis of benzothiazines **6**.

While identifying the multiple dimensions of developed approach, we have come across towards the synthesis of pyrrolo[1,2-*c*]thiazoles (**8aa** and **ai**) and thiazolo[3,4-*a*]pyridines (**8ba** and **ci**) skeletons by employing l-prolinol (**7a**), 2-piperidinemethanol (**7b**), (±)-pipecolinic acid (**7c**) derivatives and isothiocyanates **2a**, **i** as substrates (Scheme 6). The developed reaction conditions demonstrated excellent proficiency in achieving biologically potential *N*,*S*-heterocycles **8** in yields up to 94%.

Scheme 6. Synthesis of pyrrolo[1,2-*c*]thiazoles and thiazolo[3,4-*a*]pyridines.

Scheme 7. Synthesis of *N*,*S*-spiroheterocycles **10**.

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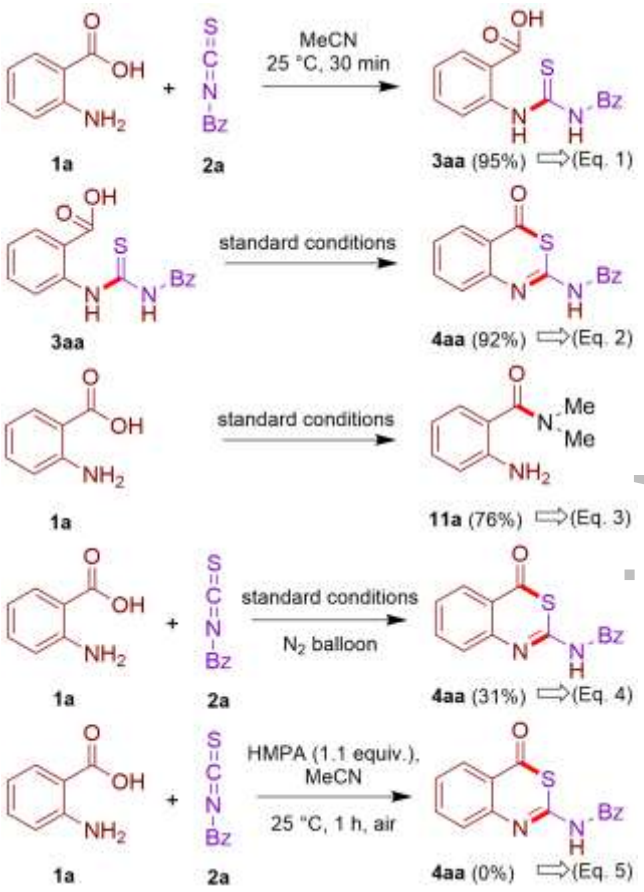
To explore the broader application of the devised method, we were encouraged to realize the amino acid derivatives **9** as starting materials to construct the rarely explored *N*,*S*-spiroheterocycles **10** (Scheme 7). Interestingly, it was found that the developed approach was equally efficient to furnish *N*,*S*-spirocyclic frameworks of various ring sizes in good yields. It was also observed that the compound **10ba** was existing in an inseparable keto-enol tautomeric form which was confirmed by NMR spectra.

After demonstrating a broad range of substrate scope, we have attempted to propose a plausible reaction mechanism for this chemical transformation. To fulfil this purpose, we have executed admissible control experiments. To begin with, we have carried out the reaction of anthranilic acid (**1a**) and benzoyl isothiocyanate (**2a**) to obtain intermediate **3aa** in 95% isolated yield under HMPT-free reaction conditions (Scheme 8, Eq. 1). The isolated intermediate **3aa** is further subjected to standard reaction conditions to obtain the desired product **4aa** in 92% yield (Scheme 8, Eq. 2). The obtained results reinforced the formation of thiourea intermediate **3aa** during the reaction pathway. Alternatively, a reaction of anthranilic acid (**1a**) under standard reaction conditions resulted in an amide derivative **11a** in 76% yield (Scheme 8, Eq. 3). The formation of amide **11a** was attributed to the acid-amine coupling reaction between anthranilic acid **1a** and the *in-situ* liberated *N*,*N*-dimethylamine (**12a**) during the reaction process. Simultaneously, we have also carried out the reaction of **1a** and **2a** under standard reaction conditions in presence of N_2 atmosphere. Surprisingly, the reaction conditions generated the desired product **4aa** with mere 31% yield (Scheme 8, Eq. 4). Finally, to elucidate the prospect of phosphine reagent under aerobic conditions, we have carried out the reaction of anthranilic acid (**1a**) and benzoyl isothiocyanate (**2a**) under HMPA-mediated reaction conditions. To our disappointment, the reaction conditions were found to be inefficient in producing **4aa** (Scheme 8, Eq. 5). The above obtained results guided us to understand the following aspects, (i) The reagent $P(NMe_2)_3$ is not getting converted to $OP(NMe_2)_3$ *via* aerial oxidation. (ii) The aerial oxygen is mandatory for acquiring the desired product in higher yields. (iii) The addition of HMPT to the reaction mixture leads to the liberation of Me_2NH (**12a**).



Scheme 8. Control experiments.

With these preliminary results in hand, we intended to gain further insights into the reaction mechanism. To achieve this motive, we have performed the reaction of anthranilic acid (**1a**) ($[M+H]^+$ = 138.0) and benzoyl isothiocyanate (**2a**) ($[M]^+$ = 162.9) under the standard reaction conditions. The course of the reaction was monitored by liquid chromatography-mass spectrometry (LC–MS) after an interval of 15 min, 30 min and 60 min. The mass-spectroscopic data revealed the possible participation of intermediates **3aa** ($[M+H]^+$ = 301.1) to obtain the desired product **4aa** ($[M+H]^+$ = 283.1) along with the formation of byproduct **C** ($[M]^+$ = 151.1) during the course of reaction (details of mass spectrometric data have been provided in Figure 1, SI).

On the basis of above experimental evidences and literature reports,[10] a plausible mechanism has been depicted (Scheme 9). According to the proposed mechanism, thiourea intermediate **3aa** ($[M+H]^+$ = 301.1) would result by the reaction of anthranilic acid (**1a**) ($[M+H]^+$ = 138.0) and benzoyl isothiocyanate (**2a**) ($[M]^+$ = 162.9). The tendency of $P(NMe_2)_3$ towards hydroxyl functionality enables the rapid discharge of *N*,*N*-dimethylamine (**12a**) moiety and subsequent oxidation of phosphine by aerial oxygen results in the formation of intermediate **A**. Next, the intramolecular heterocyclization *via* nucleophilic attack of sulphur-atom over carbonyl carbon leads to the formation of intermediate **B**. Subsequent

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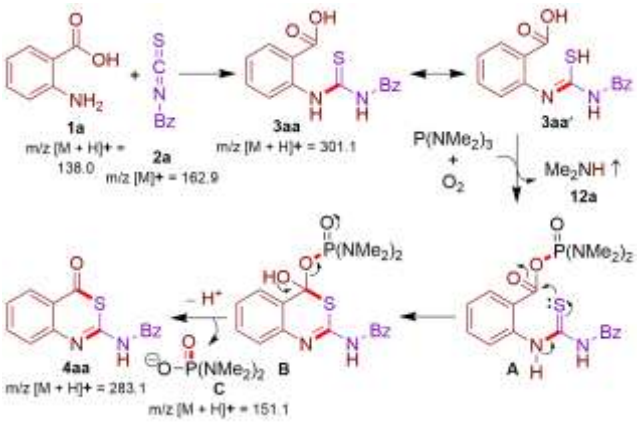
elimination of phosphorodiamidate derivative **C** ($[M]^+$ = 151.1) and deprotonation provides the desired product **4aa** ($[M+H]^+$ = 283.1).



Scheme 9. Proposed mechanism for $P(NMe_2)_3$-mediated heterocyclization reaction.

Conclusion

In conclusion, we have established a facile protocol towards the synthesis of diversified *N*,*S*-heterocycles using $P(NMe_2)_3$–mediated heterocyclization reaction between bis-nucleophiles and isothiocyanates under aerobic conditions. This process provides a convenient synthetic route to pharmaceutically valuable 2-(acyl)amino-4*H*-3,1-benzothiazin-4-ones and related thienothiazinones. The devised method was also beneficial for the synthesis of very rarely explored pyrrolo[1,2-*c*]thiazoles, thiazolo[3,4-*a*]pyridines and *N*,*S*-spiroheterocycles. The reaction conditions showed excellent functional group tolerance and delivered the desired products in yields up to 97%. The developed organophosphine-mediated approach was well understood by adequate control experiments and mass-spectroscopic data.

Experimental Section

General Information

All starting materials were purchased from commercial suppliers (Sigma-Aldrich, Alfa-Aesar, SD fine chemicals, Merck, HI Media) and were used without further purification unless otherwise indicated. All reactions were performed in a 10 mL round bottom flask with magnetic stirring. Solvents used in extraction and purification were distilled prior to use. Thin-layer chromatography (TLC) was performed on TLC plates purchase from Merck. Compounds were visualized with UV light (λ = 254 nm) and/or by immersion in $KMnO_4$ staining solution followed by heating. Products were purified by CombiFlash MPLC. Melting points were determined in open capillary tubes on EZ-Melt automated melting point apparatus and are uncorrected. All HRMS are recorded using 6545 QTOF LC/MS, Agilent instrument equipped with an auto sampler in EI-QTOF method and LC-MS are recorded in APCI method in acetonitrile solvent. ^1H (^{13}C) NMR spectra were recorded at 400 (100) MHz on a Brucker spectrometer using $CDCl_3$ and DMSO-d_6 as a solvent. The ^1H and ^{13}C chemical shifts were referenced to residual solvent signals at $\delta_{H/C}$ 7.26/77.28 ($CDCl_3$) and $\delta_{H/C}$ 2.51/39.50 (DMSO-d_6) relative to TMS as internal standards. Coupling constants J [Hz] were directly taken from the spectra and are not averaged. Splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), overlapped and br (broad).

General Experimental Procedure for the Synthesis of 4*H*-3,1-Benzothiazin-4-ones 4aa-ka and 4ab-ah

A 10 mL round bottom flask was charged with 2-amino-aryl/alkyl carboxylic acids **1a-k** (1.0 mmol), aryl or alkyl isothiocyanates **2a-h** (1.0 mmol) in MeCN (2 mL) and the reaction mixture was stirred at room temperature (25 °C) for 15 to 30 mins. The reaction progress was monitored by TLC (SiO_2, Hexane/EtOAc = 8:2) and LC-MS. The TLC and LCMS analysis showed the absence of both the starting materials and the formation of thiourea intermeiate. The reaction mixture was then added with $P(NMe_2)_3$ (1.1 mmol) and the reaction mixture was stirred at room temperature (25 °C) for 5-210 mins. After completion of the reaction (progress was monitored by TLC; SiO_2, Hexane/EtOAc = 8:2 and LC-MS), the recation mixture was extracted with ethyl acetate (3 × 15 mL), water (20 mL). The combined organic layer was washed with sodium thiosulphate solution (3 × 10 mL) and dried over anhydrous Na_2SO_4. Solvent was removed under reduced pressure and the remaining residue was purified over CombiFlash MPLC using Hexane/EtOAc = 70:30 as an eluent to obtain the desired 4*H*-3,1-benzothiazin-4-ones **4aa-ka** and **4ab-ah** in high yields.

General Experimental Procedure for the Synthesis of 2-Amino-1,3-benzothiazines 6aa-ha and 6ab-ad, ah-am

A 10 mL round bottom flask was charged with 2-amino aralkyl alcohols **5a-h** (1.0 mmol), aryl or alkyl isothiocyanates **2a-d**, **h-m** (1.0 mmol) in MeCN (2 mL) and the reaction mixture was stirred at room temperature (25 °C) for 15 to 30 mins. The reaction progress was monitored by TLC (SiO_2, Hexane/EtOAc = 8:2) and LC-MS. The TLC and LCMS analysis showed the absence of both the starting materials and the formation of thiourea intermeiate. The reaction mixture was then added with $P(NMe_2)_3$ (1.1 mmol) and the reaction mixture was stirred at room temperature (25 °C) for 15-90 mins. After completion of the reaction (progress was monitored by TLC; SiO_2, Hexane/EtOAc = 8:2 and LC-MS), the recation mixture was extracted with ethyl acetate (3 × 15 mL), water (20 mL). The combined organic layer was washed with sodium thiosulphate solution (3 × 10 mL) and dried over anhydrous Na_2SO_4. Solvent was removed under reduced pressure and the remaining residue was purified over CombiFlash MPLC using Hexane/EtOAc = 70:30 as an eluent to obtain the desired 2-amino-1,3-benzothiazines **6aa-ha** and **6ab-ad**, **ah-am** in high yields.

General Experimental Procedure for the Synthesis of Pyrrolo[1,2-*c*]thiazoles (8aa and ai) and Thiazolo[3,4-*a*]pyridines (8ba and ci)

A 10 mL round bottom flask was charged with l-prolinol (**7a**) or 2-piperidinemethanol (**7b**) or (±)-pipecolinic acid (**7c**) (1.0 mmol), bezoyl isothiocyanates (**2a**) or phenyl isothiocyanates (**2i**) (1.0 mmol) in MeCN (2 mL) and the reaction mixture was stirred at room temperature (25 °C) for 15 to 30 mins. The reaction progress was monitored by TLC (SiO_2, Hexane/EtOAc = 8:2) and LC-MS. The TLC and LCMS analysis showed the absence of both the starting materials and the formation of thiourea intermeiate. The reaction mixture was then added with $P(NMe_2)_3$ (1.1 mmol) and the reaction mixture was stirred at room temperature (25 °C) for 15-90 mins. After completion of the reaction (progress was monitored by TLC; SiO_2, Hexane/EtOAc = 8:2 and LC-MS), the recation mixture

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was extracted with ethyl acetate (3 × 15 mL), water (20 mL). The combined organic layer was washed with sodium thiosulphate solution (3 × 10 mL) and dried over anhydrous Na_2SO_4. Solvent was removed under reduced pressure and the remaining residue was purified over CombiFlash MPLC using Hexane/EtOAc = 80:20 as an eluent to obtain the desired pyrrolo[1,2-*c*]thiazoles (**8aa** and **ai**) and thiazolo[3,4-*a*]pyridines (**8ba** and **ci**) in high yields.

General Experimental Procedure for the Synthesis of *N,S*-spirocycles 10aa-da

A 10 mL round bottom flask was charged with 1-amino-1-cycloalkylcarboxylic acids **9a-d**, bezoyl isothiocyanates (**2a**) (1.0 mmol) in MeCN (2 mL) and the reaction mixture was stirred at room temperature (25 °C) for 30 mins. The reaction progress was monitored by TLC (SiO_2, Hexane/EtOAc = 8:2) and LC-MS. The TLC and LCMS analysis showed the absence of both the starting materials and the formation of thiourea intermeiate. The reaction mixture was then added with $P(NMe_2)_3$ (1.1 mmol) and the reaction mixture was stirred at room temperature (25 °C) for 15-90 mins. After completion of the reaction (progress was monitored by TLC; SiO_2, Hexane/EtOAc = 8:2 and LC-MS), the recation mixture was extracted with ethyl acetate (3 × 15 mL), water (20 mL). The combined organic layer was washed with sodium thiosulphate solution (3 × 10 mL) and dried over anhydrous Na_2SO_4. Solvent was removed under reduced pressure and the remaining residue was purified over CombiFlash MPLC using Hexane/EtOAc = 80:20 as an eluent to obtain the desired *N,S*-spirocycles **10aa-da** in high yields.

Analytical Data of Synthesized 4*H*-3,1-Benzothiazin-4-ones 4aa-ka and 4ab-ah

***N*-(4-oxo-4*H*-benzo[*d*][1,3]thiazin-2-yl)benzamide** (**4aa**) (Scheme 2): **White solid**; $\mathbf{R_f}$ = 0.60 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 262 mg (93%); **m.p** = 168.1-169.1 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 13.24 (s, 1H), 8.07 (d, *J* = 8.0 Hz, 3H), 7.90 (dt, *J* = 8.0 Hz, 1H), 7.69-7.62 (m, 2H), 7.54 (t, *J* = 8.0 Hz, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 185.11, 136.81, 133.47, 129.04, 128.96, 124.89, 119.92, 114.02 ppm; **MS** (APCI):[M + 1]$^+$ = 282.90 (99.84%); **HRMS** (EI-QTOF, [M + H]$^+$): calculated for $C_{15}H_{11}N_2O_2S$: 283.0541; found: 283.0536.

***N*-(7-methyl-4-oxo-4*H*-benzo[*d*][1,3]thiazin-2-yl)benzamide** (**4ba**) (Scheme 2): **White solid**; $\mathbf{R_f}$ = 0.60 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 275 mg (93%); **m.p** = 181.2-182.4 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 12.25 (br, 1H), 8.03 (d, *J* = 7.6 Hz, 2H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 2H), 7.43 (br, 1H), 7.33 (dd, *J* = 8.0 Hz, 1H), 2.44 (s, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 184.51, 147.8, 133.4, 132.7, 129.01, 128.91, 128.8, 124.85, 117.75, 21.88 ppm; **MS** (APCI): [M + 1]$^+$ = 297.10 (99.71%); **HRMS** (ESI-QTOF, [M + H]$^+$): calculated for $C_{16}H_{13}N_2O_2S$: 297.0697; found: 297.0690.

***N*-(7-methoxy-4-oxo-4*H*-benzo[*d*][1,3]thiazin-2-yl)benzamide** (**4ca**) (Scheme 2): **White solid**; $\mathbf{R_f}$ = 0.50 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 296 mg (95%); **m.p** = 186.2-187.4 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 12.21 (br, 1H), 8.03 (d, *J* = 7.6 Hz, 2H), 7.99 (t, *J* = 7.2 Hz, 1H),7.63 (t, *J* = 7.2 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.11 (d, *J* = 8.8 Hz, 1H), 7.04 (d, *J* = 2.4 Hz, 1H), 3.91 (s, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 183.1, 168.1, 165.7, 155.9, 149.7, 133.4, 132.7, 129.0, 128.9, 127.1, 115.7, 113.8, 110.6, 56.3 ppm; **MS** (APCI): [M + 1]$^+$ = 313.1 (99.75%); **HRMS** (ESI-QTOF, [M + H]$^+$): calculated for $C_{16}H_{13}N_2O_3S$: 313.0646; found: 313.0640.

***N*-(7-chloro-4-oxo-4*H*-benzo[*d*][1,3]thiazin-2-yl)benzamide** (**4da**) (Scheme 2): **White solid**; $\mathbf{R_f}$ = 0.50 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 284 mg (90%); **m.p** = 233.2-224.6 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 12.44 (s, 1H), 8.03-8.00 (m, 3H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.58 (d, *J* = 1.9 Hz, 1H), 7.54-7.49 (m, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 184.4, 168.18, 156.54, 148.9, 141.18, 133.53, 132.44, 129.0, 128.93, 127.8, 127.57, 126.9, 118.67 ppm; **MS** (APCI): [M + 1]$^+$ = 317.3 (100%); **HRMS** (ESI-QTOF, [M + H]$^+$): calculated for $C_{15}H_{10}ClN_2O_2S$: 317.0151; found: 317.0146.

***N*-(4-oxo-7-(trifluoromethyl)-4*H*-benzo[*d*][1,3]thiazin-2-yl)benzamide** (**4ea**) (Scheme 2): **Off-white solid**; $\mathbf{R_f}$ = 0.55 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 315 mg (90%); **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 12.48 (br, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 8.03 (d, *J* = 8 Hz, 2H), 7.84-7.80 (m, 2H), 7.65 (t, *J* = 7.2 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 2H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 184.83, 167.91, 156.2, 148.1, 135.6 (q, *J* = 32.5 Hz), 133.6, 132.23, 129.6, 129.0, 128.9, 127.7, 126.6, 124.56 (q, *J* = 272.1 Hz), 122.0, 119.5 ppm; **MS** (APCI): [M + 1]$^+$ = 351.0 (98.42%); **HRMS** (ESI-QTOF, [M + H]$^+$): calculated for $C_{16}H_{10}F_3N_2O_2S$: 351.0415; found: 351.0411.

***N*-(4-oxo-4*H*-pyrido[2,3-*d*][1,3]thiazin-2-yl)benzamide** (**4fa**) (Scheme 2): **Off-white solid**; $\mathbf{R_f}$ = 0.45 (SiO_2, Hexane/EtOAc = 7:3); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 60:40); **yield**: 229 mg (81%); **m.p** = 211.8-212.6 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 12.73 (br, 1H), 8.95 (s, 1H), 8.41 (d, *J* = 7.6 Hz, 1H), 8.07 (d, *J* = 7.6 Hz, 2H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.55-7.51 (m, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 186.2, 168.76, 157.96, 157.16, 134.38, 133.62, 132.55, 129.19, 128.96, 122.95, 115.88 ppm; **MS** (APCI): [M + 1]$^+$ = 284.10 (100.00%); **HRMS** (ESI-QTOF, [M + H]$^+$): calculated for $C_{14}H_{10}N_3O_2S$: 284.0493; found: 284.0490.

***N*-(4-oxo-4*H*-naphtho[2,3-*d*][1,3]thiazin-2-yl)benzamide** (**4ga**) (Scheme 2): **Yellow solid**; $\mathbf{R_f}$ = 0.60 (SiO_2 Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 286 mg (86%); **m.p** = 265.0-266.0 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 12.16 (br, 1H), 8.79 (s, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 8.17 (s, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 2H), 7.71 (t, *J* = 8.0 Hz, 1H), 7.66-7.58 (m, 2H), 7.53 (t, *J* = 7.6 Hz, 2H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 186.02, 171.98, 156.26, 141.99, 138.14, 135.28, 134.97, 133.71, 132.95, 132.17, 131.77 ppm; **MS** (APCI): [M + 1]$^+$ = 333.3 (99.39%); **HRMS** (ESI-QTOF, [M + H]$^+$): calculated for $C_{19}H_{13}N_2O_2S$: 333.0697; found: 333.0694.

***N*-(5,6-dimethyl-4-oxo-4*H*-thieno[2,3-*d*][1,3]thiazin-2-yl)benzamide** (**4ha**) (Scheme 2): **White solid**; $\mathbf{R_f}$ = 0.60 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 278 mg (88%); **m.p** = 251.1-252.3 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 12.39 (s, 1H), 8.01 (d, *J* = 7.2 Hz, 2H), 7.63 (t, *J* = 7.2 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 2H), 2.34 (s, 6H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 177.78, 167.07, 163.3, 157.86, 133.4, 132.33, 129.11, 128.88, 119.76 13.91, 12.7 ppm; **MS** (APCI): [M + 1]$^+$ = 317.10 (99.28%); **HRMS** (ESI-QTOF, [M + H]$^+$): calculated for $C_{15}H_{13}N_2O_2S_2$: 317.0418; found: 317.0415.

(*Z*)-*N*-(8-oxo-5,6,7,8-tetrahydro-4*H*-1,3-thiazocin-2-yl)benzamide (**4ia**) (Scheme 2): **Yellow solid**; $\mathbf{R_f}$ = 0.5 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 194 mg (74%); **m.p** = 145.2-146.9 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 12.99 (br, 1H), 7.84 (d, *J* = 7.2 Hz, 2H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.4 Hz, 2H), 4.06-4.03 (m, 2H), 2.52-2.48 (m, 2H), 1.83-1.75 (m, 4H) ppm; **MS** (APCI): [M + 1]$^+$ = 263.1 (91.6%); **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 184.6, 174.76, 167.5, 134.11, 133.9, 129.6, 129.14, 51.17, 35.27, 23.19, 20.28 ppm; **MS** (APCI): [M +

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1]$^+$ = 317.10 (99.28%); **HRMS** (ESI-QTOF, [M + H]$^+$): calculated for $C_{13}H_{15}N_2O_2S$: 263.0854; found: 263.0852.

***N*-(5-methyl-6-oxo-5,6-dihydro-4*H*-1,3-thiazin-2-yl)benzamide** (**4ja**) (Scheme 2): **Sticky solid**; **R$_f$** = 0.4 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 203 mg (82%); **m.p** = 196.0-197.1 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 11.69 (br, 1H), 7.82 (d, *J* = 7.6 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 3.96 (dd, *J* = 6, 5.6 Hz, 1H), 3.69 (t, *J* = 12.2 Hz, 1H), 3.15-3.09 (m, 1H), 1.15 (d, *J* = 7.2 Hz, 1H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 181.5, 174.4, 170.87, 134.95, 133.19, 129.7, 128.99, 50.09, 35.14, 12.36 ppm; **HRMS** (ESI-QTOF, [M + H]$^+$): calculated for $C_{12}H_{13}N_2O_2S$: 249.0697; found: 249.0694.

(*Z*)-*N*-(1-methyl-4-oxo-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)benzamide (**4ka**)[8d] (Scheme 2): **Off-white solid**; **R$_f$** = 0.4 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 258 mg (87%); **m.p** = 265.0-266.0 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 8.08 (d, *J* = 7.9 Hz, 1H), 8.02 (d, *J* = 7.6 Hz, 2H), 7.95 (t, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.69 (t, *J* = 7.2 Hz, 1H), 7.55-7.47 (m, 3H), 4.00 (s, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 173.7, 167.9, 158.6, 142.0, 137.0, 135.1, 131.93, 130.7, 129.75, 127.9, 125.57, 117.67, 117.3, 36.95 ppm; **MS** (APCI): [M + 1]$^+$ = 297.1 (93.94%); **HRMS** (ESI-QTOF, [M + H]$^+$): calculated for $C_{16}H_{13}N_2O_2S$: 297.0697; found: 297.0695.

2-(*p*-tolylamino)-4*H*-benzo[*d*][1,3]thiazin-4-one (**4ab**)[11] (Scheme 3): **White solid**; **R$_f$** = 0.4 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 241 mg (90%); **m.p** = 160.6-161.2 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 10.11 (br, 1H), 7.95 (d, *J* = 8 Hz, 1H), 7.73 (t, *J* = 8 Hz, 1H), 7.67 (d, *J* = 8 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.16 (d, *J* = 8 Hz, 2H), 2.27 (s, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 184.04, 152.2, 150.3, 137.2, 136.7, 133.18, 129.7, 128.81, 124.92, 124.8, 121.0, 117.73, 20.9 ppm; **MS** (APCI): [M + 1]$^+$ = 269.0 (93.17%); **HRMS** (ESI-QTOF, [M + H]$^+$): calculated for $C_{15}H_{13}N_2OS$: 269.0748; found: 269.0744.

2-((2,4-dimethylphenyl)amino)-4*H*-benzo[*d*][1,3]thiazin-4-one (**4ac**) (Scheme 3): **White solid**; **R$_f$** = 0.4 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 254 (90%); **m.p** = 140.0-141.0 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 9.80 (br, 1H), 7.90 (br, 1H), 7.66 (t, *J* = 7.6 Hz, 1H),7.27 (d, *J* = 8.0 Hz, 1H), 7.22-7.15 (m, 3H), 7.02 (br, 1H), 2.26 (s, 3H), 2.16 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 183.9, 155.38, 150.72, 136.72,136.2, 131.0, 127.85, 124.98, 124.2, 117.36, 20.92, 17.85 ppm; **MS** (APCI): [M + 1]$^+$= 283.20 (99.43%); HRMS (ESI-QTOF, [M + H]$^+$): calculated for $C_{16}H_{15}N_2OS$: 283.0905; found: 283.0901.

2-((2-methoxyphenyl)amino)-4*H*-benzo[*d*][1,3]thiazin-4-one (**4ad**) (Scheme 3): **White solid**; **R$_f$** = 0.5 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 273 mg (96%); **m.p** = 176.0-177.0 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 9.61 (br, 1H), 7.92 (d, *J* = 6.8 Hz, 1H), 7.78 (br, 1H), 7.69 (t, *J* = 6.8 Hz, 1H), 7.34 (t, *J* = 8 Hz, 1H), 7.24-7.19 (m, 2H), 7.09 (d, *J* = 8.4 Hz, 1H), 6.97 (t, *J* = 7.2 Hz, 1H), 3.80 (s, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 184.25, 154.65, 152.83, 150.41, 136.69, 128.54, 127.0, 126.3, 124.86, 124.5, 120.93, 117.53, 112.44, 56.14 ppm; **MS** (APCI): [M + 1]$^+$ = 285.10 (99.73%); **HRMS** (ESI-QTOF, [M + H]$^+$): calculated for $C_{15}H_{13}N_2O_2S$: 285.0697; found: 285.0691.

2-((3-methoxyphenyl)amino)-4*H*-benzo[*d*][1,3]thiazin-4-one (**4ae**) (Scheme 3): **White solid**; **R$_f$** = 0.5 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 261 mg (92%); **m.p** = 177.5-178.5 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 10.19 (br, 1H), 7.97 (d, *J* = 7.2 Hz, 1H), 7.75 (t, *J* = 7.2 Hz, 1H), 7.62 (s, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.34-7.22 (m, 3H), 6.67 (d, *J* = 8.0 Hz, 1H), 3.77 (s, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 183.99, 160.0, 151.96, 150.0, 140.98, 136.8, 130.0, 128.92, 125.28, 124.81, 117.82, 112.87, 109.58, 106.46, 55.47 ppm; **MS** (APCI): [M + 1]$^+$ = 285.1 (99.70%); **HRMS** (ESI-QTOF, [M + H]$^+$): calculated for $C_{15}H_{13}N_2O_2S$: 285.0697; found: 285.0693.

2-((3-fluorophenyl)amino)-4*H*-benzo[*d*][1,3]thiazin-4-one (**4af**) (Scheme 3): **White solid**; **R$_f$** = 0.5 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 245 mg (90%); **m.p** = 188.2-188.4 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 10.38 (br, 1H), 7.99 (d, *J* = 7.6 Hz, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.77 (t, *J* = 7.2 Hz, 1H), 7.55-7.50 (m, 2H), 7.41-7.33 (m, 2H), 6.90 (dt, *J* = 7.6, 2.0 Hz, 1H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 183.7, 162.55 (d, *J* = 240.2 Hz), 151.8, 149.65, 141.57, 141.46, 136.8, 130.84, 130.75, 129.0, 125.59, 124.82, 117.9, 116.17, 110.18 (d, *J* = 20.9 Hz), 107.37 (d, *J* = 26.4 Hz) ppm; **MS** (APCI): [M + 1]$^+$ = 273.20 (96.45%); **HRMS** (ESI-QTOF, [M + H]$^+$): calculated for $C_{14}H_{10}FN_2OS$: 273.0497; found: 273.0494.

2-((4-(trifluoromethyl)phenyl)amino)-4*H*-benzo[*d*][1,3]thiazin-4-one (**4ag**) (Scheme 3): **Off-white solid**; **R$_f$** = 0.60 (SiO_2, Hexane/EtOAc = 7:3); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 70:30); **yield**: 296 mg (92%); **m.p** = 220-220.8 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 10.53 (br, 1H), 8.06 (d, *J* = 6.8 Hz, 2H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.79 (t, *J* = 7.2 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 2H), 7.57 (d, *J* = 8.0Hz, 1H), 7.37 (t, *J* = 6.8 Hz, 1H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 183.66, 151.69, 149.39, 143.44, 136.72, 129.0, 126.45, 125.7, 125.21 (q, *J* = 249.8 Hz), 123.21 (q, *J* = 31.8 Hz), 120.27, 117.94 ppm; **MS** (APCI): [M + 1]$^+$ = 323.0 (99.73%); **HRMS** (ESI-QTOF, [M + H]$^+$): calculated for $C_{15}H_{10}F_3N_2OS$: 323.0465; found: 323.0460.

Ethyl (4-oxo-4*H*-benzo[*d*][1,3]thiazin-2-yl)carbamate (**4ah**) (Scheme 3): **Off-white solid**; **R$_f$** = 0.5 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 70:30); **yield**: 220 mg (88%), **m.p** = 111.8-113.0 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 11.69 (br, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.83 (dt, *J* = 6.8, 1.2 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 1.23 (t, *J* = 7.2 Hz, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 183.91, 153.44, 152.29, 147.59, 135.72, 128.95, 126.89, 125.0, 119.52, 62.79, 14.19 ppm; **MS** (APCI): [M+ 1]$^+$ = 251.0 (99.45%); **HRMS** (ESI-QTOF, [M + H]$^+$): calculated for $C_{11}H_{11}N_2O_3S$: 251.0490; found: 251.0488.

Analytical Data of Synthesized 2-Amino-1,3-benzothiazines 6aa-ha and 6ab-ad, ah-am

***N*-(4*H*-Benzo[*d*][1,3]thiazin-2-yl)benzamide** (**6aa**)[2f] (Scheme 4); **White solid**; **R$_f$** = 0.60 (SiO_2, hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (hexane/EtOAc = 87:13); **yield**: 260 mg (97%); **m.p** 124-125 °C (Lit[2f] 123-124 °C); **^{1}H NMR** (400 MHz, DMSO d_6) δ = 11.69 (br s, 1H), 8.07 (d, *J* = 7.6 Hz, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.30-7.24 (m, 2H), 7.20 (dd, *J* = 8.0 Hz, 1H), 7.13 (t, *J* = 8.0 Hz, 1H), 3.95 (s, 2H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 172.4 (less intense), 164.5 (less intense), 138.4 (less intense), 135.7 (less intense), 132.55, 129.31, 128.75, 128.54, 127.36, 125.24, 121.66, 28.21 ppm; **HRMS** (ESI-QTOF, [M + H]+): calcd for $C_{15}H_{13}N_2OS$, 269.0748; found, 269.0746.

***N*-(7-methyl-4*H*-benzo[*d*][1,3]thiazin-2-yl)benzamide** (**6ba**)[2f] (Scheme 4): **Off-white solid**; **R$_f$** = 0.60 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (EtOAc/Hexane = 20:80); **yield**: 259 mg (92%); **m.p** = 144.6-145.4 °C (Lit[2f] 145-146 °C); **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 11.61 (br, 1H), 8.07 (d, *J* = 7.2 Hz,

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2H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.12 (d, *J* = 2.4 Hz, 1H), 7.00 (brs, 1H), 6.94 (dd, *J* = 7.6, 2.2 Hz, 1H), 3.90 (s, 2H), 2.27 (s, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 170.2 (less intense), 137.9, 135.8, 132.5, 129.32, 128.73, 127.18, 125.86, 118.64, 28.0, 21.27 ppm; **MS** (APCI): $[M + 1]^+$ = 283.1 (99%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{16}H_{15}N_2OS$: 283.0905; found: 283.0900.

***N*-(8-methyl-4*H*-benzo[*d*][1,3]thiazin-2-yl)benzamide** (**6ca**)[2f] (Scheme 4): **Off-white solid**; **R_f** = 0.60 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 251 mg (89%); **m.p** = 128.0-129.2 °C (Lit[2f] 127-128 °C); **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 11.59 (br, 1H), 8.02 (d, *J* = 5.6 Hz, 2H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.17-7.14 (m, 1H), 7.05 (d, *J* = 4.9 Hz, 2H), 3.93 (s, 2H), 2.31 (s, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 170.1 (less intense), 138.7 (less intense), 134.5 (less intense), 132.81, 129.97, 129.13, 128.79, 125.75, 124.98, 28.82, 17.74 ppm; **MS** (APCI): $[M + 1]^+$ = 283.1 (99.10%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{16}H_{15}N_2OS$: 283.0905; found: 283.0902.

***N*-(8-fluoro-4*H*-benzo[*d*][1,3]thiazin-2-yl)benzamide** (**6da**)[2f] (Scheme 4): **Off-white solid**; **R_f** = 0.50 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 235 mg (82%); **m.p** = 124.6-125.8 °C (Lit[2f] 124-125 °C); **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 11.95 (s, 1H), 8.00 (d, *J* = 7.9 Hz, 2H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.19-7.16 (m, 2H), 7.08-7.05 (m, 1H), 3.97 (s, 2H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 172.0 (less intense), 133.05 129.07, 128.97, 128.83, 125.59 (d, *J* = 232 Hz), 122.93 (d, *J* = 3 Hz), 115.27 (d, *J* = 20 Hz), 28.12 ppm; **MS** (APCI): $[M + 1]^+$ = 287.0 (99.2%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{15}H_{12}FN_2OS$: 287.0654; found: 287.0650.

***N*-(7-chloro-4*H*-benzo[*d*][1,3]thiazin-2-yl)benzamide** (**6ea**)[2f] (Scheme 4): **White solid**; **R_f** = 0.60 (SiO_2, EtOAc/Hexane = 8:2); **purification system**: CombiFlash MPLC (EtOAc/Hexane = 20:80); **yield**: 266 mg (88%); **m.p** = 152.2-153.4 °C (Lit[2f] 151-152 °C); **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 11.71 (br, 1H), 8.05 (d, *J* = 7.6 Hz, 2H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 1H) 7.19 (br, 2H), 3.95 (s, 2H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 136.3 (less intense), 132.76, 132.57, 129.39, 128.97, 128.81, 124.9, 120.6, 27.65 ppm; **MS** (APCI): $[M + 1]^+$ = 303.0 (99.80%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{15}H_{12}ClN_2OS$: 303.0358; found: 303.0354.

***N*-(7-(trifluoromethyl)-4*H*-benzo[*d*][1,3]thiazin-2-yl)benzamide** (**6fa**)[2f] (Scheme 4): **White solid**; **R_f** = 0.50 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 296 mg (88%); **m.p** = 116.6-117.8 °C (Lit[2f] 116-117 °C); **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 11.84 (br, 1H), 8.05 (d, *J* = 7.2 Hz, 2H), 7.58 (t, *J* = 7.2 Hz, 1H), 7.51-7.45 (m, 5H), 4.05 (s, 2H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 134.8 (less intense), 132.84, 129.72, 129.3, 129.2 (q, *J* = 31.8 Hz), 128.5, 126.12, 124.38 (q, *J* = 271 Hz), 121.7, 27.94 ppm; **MS** (APCI): $[M + 1]^+$ = 337.0 (98.57%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{16}H_{12}F_3N_2OS$: 337.0622; found: 337.0618.

***N*-(4-phenyl-4*H*-benzo[*d*][1,3]thiazin-2-yl)benzamide** (**6ga**) (Scheme 4): **Off-White solid**; **R_f** = 0.50 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 258 mg (75%); **m.p** = 87.0-88.0 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 11.65 (br, 1H), 8.01 (d, *J* = 8.0 Hz, 2H), 7.53 (dd, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 7.9 Hz, 2H), 7.38-7.28 (m, 4H), 7.25-7.09 (m, 5H), 5.57 (s, 1H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 171.1, 141.37, 134.98, 132.68, 131.32, 129.19, 128.96, 128.77, 128.06, 127.86, 127.66, 125.88, 123.89, 121.27, 44.7 ppm; **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{21}H_{17}N_2OS$: 345.1061; found: 345.1063.

(*Z*)-*N*-(1-methyl-1,4-dihydro-2*H*-benzo[*d*][1,3]thiazin-2-ylidene)benzamide (**6ha**) (Scheme 4): **Pale brown solid**; **R_f** = 0.50 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 85:15); **yield**: 260 mg (92%); **m.p** = 178.8-181 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 8.17 (d, *J* = 7.9 Hz, 2H), 7.61 (tt, *J* = 7.3 Hz, 1H), 7.52 (t, *J* = 7.9 Hz, 2H), 7.45-7.37 (m, 3H), 7.25 (dt, *J* = 7.8 Hz, 1H), 3.93 (s, 2H), 3.82 (s, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 174.1, 167.11, 140.58, 136.44, 132.68, 129.74, 128.87, 128.61, 126.87, 126.54, 125.21, 118.72, 37.82, 28.07 ppm; **MS** (APCI): $[M + 1]^+$ = 283.1 (99.42%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{16}H_{15}N_2OS$: 283.0905; found: 283.0901.

***N*-(*p*-tolyl)-4*H*-benzo[*d*][1,3]thiazin-2-amine** (**6ab**)[2f] (Scheme 5): **Off-white solid**; **R_f** = 0.60 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (EtOAc /Hexane= 20:80); **yield**: 229 mg (90%); **m.p** = 187.5-188.8 °C (Lit[2f] 188-189 °C); **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 9.35 (br, 1H), 7.70 (br, 2H), 7.22-7.15 (m, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 7.03-6.97 (m, 2H), 3.99 (s, 2H), 2.23 (s, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 150.7 (less intense), 145.0 (less intense), 131.67, 129.49, 128.34, 127.23, 123.63, 120.77, 120.29, 29.12, 20.88 ppm; **MS** (APCI): $[M + 1]^+$ = 255.1 (99.10%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{15}H_{15}N_2S$: 255.0955; found: 255.0951.

***N*-(2,4-dimethylphenyl)-4*H*-benzo[*d*][1,3]thiazin-2-amine** (**6ac**)[2f] (Scheme 5): **Off-white solid**; **R_f** = 0.45 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 231 mg (86%); **m.p** = 176.4-177.6 °C (Lit[2f] 176-177 °C); **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 9.96 (br, 1H), 7.19-7.14 (m, 2H), 7.02 (d, *J* = 2.6 Hz, 1H), 6.98 (d, *J* = 7.6 Hz, 1H), 6.91 (t, *J* = 7.4 Hz, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.72 (br, 1H), 3.92 (s, 2H), 2.21 (s, 3H), 2.07 (S, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 152.48, 135.4, 130.37, 128.34, 127.16, 124.75, 122.3, 120.92, 28.78, 21.08, 17.94 ppm; **MS** (APCI): $[M + 1]^+$ = 269.1 (98.10%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{16}H_{17}N_2S$: 269.1112; found: 269.1114.

***N*-(2-methoxyphenyl)-4*H*-benzo[*d*][1,3]thiazin-2-amine** (**6ad**)[2f] (Scheme 5): **White solid**; **R_f** = 0.60 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (EtOAc /Hexane= 20:80); **yield**: 238 mg (88%); **m.p** = 117.2-118.1 °C (Lit[2f] 116-118 °C); **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 9.15 (br, 1H), 7.46 (br, 1H), 7.21-7.15 (m, 2H), 7.04-6.93 (m, 4H), 6.89-6.85 (dt, *J* = 8.0 Hz, 1H), 3.93 (s, 2H), 3.75 (s, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d6) δ = 152.1, 151.03, 128.35, 127.2, 124.34, 123.23, 122.87, 120.91, 120.7, 111.82, 55.92, 28.9 ppm; **MS** (APCI): $[M + 1]^+$ = 271.1 (98%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{15}H_{15}N_2OS$: 271.0905; found: 271.0908.

Ethyl(4*H*-benzo[d][1,3]thiazin-2-yl)carbamate (**6ah**)[2f] (Scheme 5): **White solid**; **R_f** = 0.60 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 90:10); **yield**: 208 mg (88%); **m.p** = 92-93 °C (Lit[2f] 93-94 °C); **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 11.10 (br, 1H), 7.25-7.19 (m, 2H), 7.10-7.04 (m, 2H), 4.06 (q, *J* = 7.8 Hz, 2H), 3.94 (s, 2H), 1.18 (t, *J* = 8.0 Hz, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 157.6 (less intense), 139.98, 128.52, 127.27, 125.1, 120.88, 61.28, 28.07, 14.84 ppm; **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{11}H_{13}N_2O_2S$: 237.0697; found: 237.0694.

***N*-phenyl-4*H*-benzo[*d*][1,3]thiazin-2-amine** (**6ai**)[2f] (Scheme 5): **Off-White solid**; **R_f** = 0.60 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 85:15); yield: 221 mg (92%); **m.p** = 202.2 – 203.4 °C (Lit[2f] 201-202 °C); **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 9.43 (br, 1H), 7.84 (br, 2H),

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7.27 (t, *J* = 8.0 Hz, 2H), 7.23-7.16 (m, 2H), 7.06-6.96 (m, 3H), 4.00 (s, 2H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 152.0 (less intense), 142.9 (less intense), 129.0, 128.37, 127.26, 124.69, 123.92, 122.78, 120.77, 120.09, 29.11 ppm; **MS** (APCI): $[M + 1]^+$ = 241.1 (98.2%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{14}H_{13}N_2S$: 241.0799; found: 241.0796.

***N*-(*o*-tolyl)-4*H*-benzo[*d*][1,3]thiazin-2-amine (6aj)**[2f] (Scheme 5): **White solid**; **R_f** = 0.60 (SiO_2, EtOAc/Hexane = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 85:15); **yield**: 234 mg (92%); **m.p** = 168.8-169.8 °C (Lit[2f] 168-169 °C); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 10.00 (br, 1H), 7.19-7.15 (m, 3H), 7.09 (t, *J* = 8.0 Hz, 1H), 7.00-6.90 (m, 4H), 3.93 (s, 2H), 2.13 (s, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 152.53, 130.52, 128.35, 127.17, 126.45, 124.04, 122.32, 120.93, 28.77, 18.37 ppm; **MS** (APCI): $[M + 1]^+$ = 254.82 (99.20%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{15}H_{15}N_2S$: 255.0955; found: 255.0954.

***N*-(4-methoxyphenyl)-4*H*-benzo[*d*][1,3]thiazin-2-amine (6ak)**[2f] (Scheme 5): **Pinkish solid**; **R_f** = 0.55 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 85:15); yield: 251 mg (93%); **m.p** = 179.6-180.8 °C (Lit[2f] 170-180 °C); **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 9.29 (br, 1H), 7.74 (br, 2H), 7.21-7.14 (m, 2H), 7.01-6.99 (m, 2H), 6.86 (dd, *J* = 8.2 Hz, 2H), 3.98 (s, 2H), 3.71 (s, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 155.19, 150.2 (less intense), 145.2 (less intense), 128.32, 127.22, 121.84, 120.79, 114.18, 55.61, 29.13 ppm; **MS** (APCI): $[M + 1]^+$ = 271.1 (99.20%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{15}H_{15}N_2OS$: 271.0905; found: 271.0904.

***N*-(pyridin-3-yl)-4*H*-benzo[*d*][1,3]thiazin-2-amine (6al)**[2f] (Scheme 5): **Brown solid**; **R_f** = 0.2 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 70:30); **yield**: 202 mg (84%); **m.p** = 146.2-147.4 °C (Lit[2f] 145-146 °C); **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 9.67 (br, 1H), 8.94 (br, 1H), 8.34 (br, 1H), 8.19 (d, *J* = 7.6 Hz, 1H), 7.32-7.30 (m, 1H), 7.26-7.18 (m, 2H), 7.07-7.0 (m, 2H), 4.04 (s, 2H) ppm; **^{13}C NMR** (100 MHz, DMSO-d6) δ = 150.8 (less intense), 143.63, 141.59, 128.48, 127.32, 124.45, 123.88, 120.71, 29.02 ppm; **MS** (APCI): $[M + 1]^+$ = 242.10 (99.85%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{13}H_{12}N_3S$: 242.0751; found: 242.0747.

Ethyl 3-((4*H*-benzo[*d*][1,3]thiazin-2-yl)amino)propanoate (6am)[2f] (Scheme 5): **White solid**; **R_f** = 0.60 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 224 mg (85%); **m.p** = 60-61 °C (Lit[2f] 59-60 °C); **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 7.36 (br, 1H), 7.16-7.08 (m, 2H), 6.91 (t, *J* = 8.0 Hz, 2H), 4.05 (q, *J* = 7.6 Hz, 2H), 3.87 (s, 2H), 3.55 (t, *J* = 6.8 Hz, 2H), 2.60 (t, *J* = 7.8 Hz, 2H), 1.16 (t, *J* = 8.0 Hz, 3H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 171.78, 153.27, 146.31, 128.21, 127.1, 124.22, 122.82, 120.62, 60.34, 38.16, 34.12, 29.04, 14.53 ppm; **MS** (APCI): $[M + 1]^+$ = 265.1 (99.20%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{13}H_{17}N_2O_2S$: 265.1010; found: 265.1003.

Analytical Data of Synthesized Pyrrolo[1,2-c]thiazoles (8aa and ai) and Thiazolo[3,4-a]pyridines (8ba and ci)

(*E*)-*N*-(tetrahydropyrrolo[1,2-*c*]thiazol-3(1*H*)-ylidene)benzamide (8aa) (Scheme 6): **Off- white solid**; **R_f** = 0.6 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 229 mg (93%); **m.p** = 124.2-125.1 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 8.10 (d, *J* = 7.8 Hz, 2H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 4.31-4.22 (m, 1H), 3.70-3.63 (m, 1H), 3.42 (dt, *J* = 8.0 Hz, 1H), 3.30 (t, *J* = 9.0 Hz, 1H), 3.01 (t, *J* = 11.2 Hz, 1H), 2.29-2.03 (m, 3H), 1.67-1.55 (m, 1H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 173.46, 167.08, 136.88, 132.2, 129.41, 128.54, 64.17, 42.58, 33.31, 30.18, 27.46 ppm; **MS** (APCI): $[M + 1]^+$ = 247.1 (99.00%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{13}H_{15}N_2OS$: 247.0905; found: 247.0901.

(*E*)-*N*-(tetrahydropyrrolo[1,2-*c*]thiazol-3(1*H*)-ylidene)aniline (8ai) (Scheme 6): **White solid**; **R_f** = 0.4 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 192 mg (88%); **m.p** = 101.0-102.2 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 7.27 (t, *J* = 7.6 Hz, 2H), 7.01 (t, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 7.6 Hz, 1H), 4.27-4.19 (m, 1H), 3.61-3.54 (m, 1H), 3.42-3.35 (m, 1H), 3.29-3.23 (m, 1H), 3.05 (t, *J* = 8.4 Hz, 1H), 2.25-2.00 (m, 3H), 1.65-1.55 (m, 1H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 156.33, 129.15, 122.78, 122.00, 64.65, 45.85, 33.44, 30.41, 27.58 ppm; **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{12}H_{15}N_2S$: 219.0955; found: 219.0952.

(*E*)-*N*-(tetrahydro-1*H*-thiazolo[3,4-*a*]pyridin-3(5*H*)-ylidene)aniline (8ba) (Scheme 6): **White solid**; **R_f** = 0.6 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 218 mg (84%); **m.p** = 116.2-117.4 °C; **^{1}H NMR** (400 MHz, $CDCl_3$)) δ = 8.26 (d, *J* = 7.6 Hz, 2H), 7.47 (t, *J* = 8.0 Hz, 1H), 7.40 (t, *J* = 8.0 Hz, 2H), 4.82 (dd, *J* = 8.6 Hz, 1H), 4.65 (ddd, *J* = 8.4 Hz, 1H), 4.29 (dd, *J* = 8.1 Hz, 1H), 2.82 (t, *J* = 7.9 Hz, 1H), 2.01-1.96 (m, 2H), 1.81 (d, *J* = 8.1 Hz, 1H),), 1.56-1.46 (m, 3H), 1.26 (d, *J* = 9.2 Hz, 1H) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 175.94, 172.05, 136.85, 131.68, 129.53, 127.9, 60.24, 46.3, 33.48, 32.1, 24.3, 23.87 ppm; **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{14}H_{17}N_2OS$: 261.1061; found: 261.1055.

(*E*)-3-(phenylimino)hexahydro-1*H*-thiazolo[3,4-*a*]pyridin-1-one (8ci) (Scheme 6): **White solid**; **R_f** = 0.4 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 231 mg (94%); **m.p** = 155.4-156.2 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 7.52-7.42 (m, 3H), 7.34-7.30 (m, 2H), 4.67 (dd, *J* = 9.1, 4.4 Hz, 1H), 4.39 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.15 (dt, *J* = 12.9, 3.2 Hz, 1H), 2.16-2.11 (m, 1H), 1.95-1.80 (m, 2H), 1.69-1.52 (m, 2H), 1.43 (ddd, *J* = 16.3, 12.7 6.3 Hz, 1H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 179.04, 173.55, 134.20, 129.34, 129.14, 129.05, 60.34, 43.85, 27.78, 25.14, 22.59 ppm; **MS** (APCI): $[M + 1]^+$ = 247.1 (99.08%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{13}H_{15}N_2OS$: 247.0905; found: 247.0901.

Analytical Data of Synthesized *N*,*S*-spirocycles 10aa-da

***N*-(7-oxo-6-thia-4-azaspiro[2.4]hept-4-en-5-yl)benzamide (10aa)** (Scheme 7): **White solid**; **R_f** = 0.4 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 172 mg (70%); **m.p** = 143.2-144.4 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 12.19 (br, 1H), 8.00 (d, *J* = 7.6 Hz, 2H), 7.62 (t, *J* = 7.0 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 1.77 (d, *J* = 3.2 Hz, 2H), 1.64 (d, *J* = 4.0 Hz, 2H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 181.97, 168.96, 168.30, 133.47, 132.50, 129.0, 128.85, 57.30, 21.51, 15.85 ppm; **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{12}H_{11}N_2O_2S$: 247.0541; found: 247.0543.

***N*-(8-oxo-7-thia-5-azaspiro[3.4]oct-5-en-6-yl)benzamide (10ba)** (Scheme 7): **Brown sticky liquid**; **R_f** = 0.45 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 161 mg (62 %); **^{1}H NMR** (Keto form) (400 MHz, DMSO-d_6) δ = 10.97 (br, 1H), 7.96 (d, *J* = 8.0 Hz, 2H), 7.61 (t, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 7.9 Hz, 2H), 2.73-2.63 (m, 2H), 2.32-2.24 (m, 2H), 1.97-1.89 (m, 2H) ppm; **^{13}C NMR** (Keto form) (100 MHz, DMSO-d_6) δ = 179.36, 173.46, 168.44, 133.31, 131.59, 128.92, 128.82, 61.51, 31.31, 15.76 ppm; **^{1}H NMR** (Enol form) (400 MHz, DMSO-d_6) δ = 10.62 (br, 1H), 7.84 (d, *J* = 6.8 Hz, 2H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.41 (t, *J* = 7.9 Hz, 2H), 2.73-2.63 (m, 2H), 2.32-2.24 (m, 2H), 1.97-1.89 (m, 2H) ppm; **^{13}C NMR** (Enol form) (100 MHz, DMSO-d_6) δ = 179.36, 173.46, 168.29, 134.72, 132.84, 128.59, 127.86,

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61.51, 31.31, 15.76 ppm; **MS** (APCI): $[M + 1]^+$ = 261.9 (98.18%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{13}H_{13}N_2O_2S$: 261.0697; found: 261.0694.

***N*-(4-oxo-3-thia-1-azaspiro[4.4]non-1-en-2-yl)benzamide** (**10ca**) (Scheme 7): **brown sticky solid**; R_f = 0.4 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 203 mg (74%); **m.p** = 112.2-113.4 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 12.10 (br, 1H), 8.03 (d, *J* = 7.2 Hz, 2H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 2.05-1.92 (m, 2H), 1.92-1.76 (m, 6H) ppm; **MS** (APCI): $[M + 1]^+$ = 275.1 (94.86%); **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{14}H_{15}N_2O_2S$: 275.0854; found: 275.0852.

***N*-(5'-oxo-5'*H*-spiro[adamantane-2,4'-thiazol]-2'-yl)benzamide** (**10da**) (Scheme 7): **White solid**; R_f = 0.4 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 238 mg (70%); **m.p** = 96.3-97.4 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 11.71 (br, 1H), 8.03 (d, *J* = 8.0 Hz, 2H), 7.60 (t, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 7.9 Hz, 2H), 2.40 (dd, *J* = 13.8 Hz, 4H), 1.86-1.50 (m, 10H) ppm; **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 172.24, 133.21, 129.06, 128.99, 128.83, 38.21, 34.89, 34.64, 30.99, 27.31, 26.06 ppm; **HRMS** (ESI-QTOF, $[M + H]^+$): calculated for $C_{19}H_{21}N_2O_2S$: 341.1323; found: 341.1320.

Analytical Data of Isolated Intermediates 3aa and 11a

2-(3-Benzoylthioureido)benzoic acid (**3aa**)[12] (Scheme 8): **White solid**; R_f = 0.15 (SiO_2, Hexane/EtOAc = 6:4); **purification system**: CombiFlash MPLC (DCM/MeOH = 98:2); **yield**: 285 mg (95%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 13.36 (s, 1H), 13.17 (s, 1H), 11.56 (s, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 7.99 (d, *J* = 8.0 Hz, 2H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.69-7.61 (m, 2H), 7.54 (t, *J* = 8.0 Hz, 2H), 7.38 (t, *J* = 8.0 Hz, 1H) ppm; **MS** (APCI):[M + 1]+ = 301.1 (99.84%); **HRMS** (EI-QTOF, [M + H]+): calculated for $C_{15}H_{13}N_2O_3S$: 301.0646; found: 301.0641.

2-Amino-N,N-dimethylbenzamide (**11a**)[13] (Scheme 8): **White solid**; R_f = 0.25 (SiO_2, Hexane/EtOAc = 8:2); **purification system**: CombiFlash MPLC (Hexane/EtOAc = 80:20); **yield**: 125 mg (76%); **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 7.05 (t, *J* = 8.0 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.67 (d, *J* = 8.0 Hz, 1H), 6.52 (t, *J* = 8.0 Hz, 1H), 5.11 (s, 2H), 2.44 (s, 6H) ppm; **MS** (APCI):[M + 1]+ = 165.1 (100%); **HRMS** (EI-QTOF, [M + H]+): calculated for $C_9H_{13}N_2O$: 165.1027; found: 165.1023.

Acknowledgements

C.C.M. thank Science and Engineering Research Board (SERB), Govt. of India for financial support in the form of research grant ECR/2016/000337 and CRG/2020/004509. CCM also acknowledge Technical Education Quality Improvement Program, Phase-III and NIT Manipur for financial and research support under Minor Research Grant. S.P, V.P.R.K.P. and P.P.P. grateful to CHRIST (Deemed to be University) for their valuable research support. R.G. grateful to Ministry of Education, New Delhi for fellowship support.

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10.1002/adsc.202001149

FULL PAPER

P(III)-Mediated Cascade C-N/C-S Bond Formation: An Efficient Protocol Towards the Synthesis of *N*,*S*-Heterocycles and Spiro Compounds

Adv. Synth. Catal. **Year**, *Volume*, Page – Page

Saibabu Polina,[a] V. P. Rama Kishore Putta,[a] Raghuram Gujjarappa,[b] Virender Singh,[c] Prasad Pralhad Pujar,[a]* and Chandi C. Malakar[b]*

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