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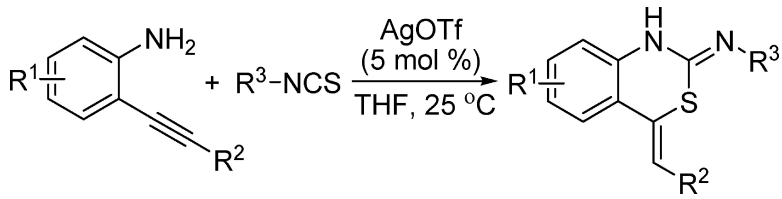

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A Facile Route to 2,4-Dihydro-1*H*-benzo[*d*][1,3]thiazines via Silver-Catalyzed Tandem Addition-Cyclization Reactions

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Tandem addition-cyclization reactions of 2-alkynylbenzenamines with isothiocyanates catalyzed by silver triflate are described; they provide an efficient and practical route for the synthesis of 2,4-dihydro-1*H*-benzo[*d*][1,3]thiazines.

Introduction

For chemistry to have its maximal effect on biology, efficient methods for the discovery of *N*-heterocyclic small molecules are in great demand in the field of chemical genetics.[1] As a privileged fragment, 2,4-dihydro-1*H*-benzo[*d*][1,3]thiazine is found in many compounds with remarkable biological activities or as subunit which acts as organic electroluminescent device.[2] As part of a continuing effort in our laboratory toward the development of new methods for the expeditious synthesis of biologically relevant heterocyclic compounds,[3] we became interested in the possibility of developing novel and efficient method to construct the 2,4-dihydro-1*H*-benzo[*d*][1,3]thiazine scaffold, with a hope of finding more active hits or leads for our particular biological assays.[4] Herein, we would like to disclose our recent efforts for the synthesis of 2,4-dihydro-1*H*-benzo[*d*][1,3]thiazines via AgOTf-catalyzed reaction of 2-alkynylbenzenamine with isothiocyanate.

Over the past decades, the use of silver catalysts in synthetic organic chemistry has become well-established as a result of the ability of silver salt to selectively activate particular functional groups under mild reaction conditions.[5] For instance, silver(I) salts have shown mild Lewis acidity and have been used as catalysts for intramolecular cyclization reactions, which take advantage of its affinity for carbon−carbon unsaturated bonds.[6] The possible mechanism was generally explained via nucleophilic addition onto Ag(I)-activated carbon−carbon unsaturated bond. This formed Ag(I)-complex renders the carbon−carbon unsaturated bond moiety electrophilic, which triggers intramolecular attack of the nucleophile, giving rise to the corresponding intermediate. Subsequently, protonolysis of the intermediate lead to recovery of the Ag(I)-salt and concomitant formation of the desired product. In our previous reports,[3a,b,e] we found that *o*-alkynylbenzaldehyde was a versatile building block in multicomponent reactions for the construction of 1,2-dihydroisoquinoline skeleton. Prompted by these results, we envisioned that 2-alkynylbenzenamine could be also used as starting material due to the structural similarity for synthesis of *N*-heterocycles via tandem addition-cyclization reaction to generate the expected molecules (Scheme 1).

Result and Discussion

To verify the practicability of the projected route as shown in Scheme 1, a set of experiments were carried out using 2-alkynylbenzenamine **1a** and phenyl isothiocyanate **2a** as model substrates. This preliminary survey, carried out in the presence of silver triflate as the catalyst at 25 °C, allowed us to evaluate and optimize the most efficient catalytic system (Table 1, entries 1−7).

To our delight, in an initial experiment, we observed the formation of the desired product **3a** (66% yield) when the reaction was performed in 1,2-dichloroethane catalyzed by AgOTf (10 mol %) (Table 1, entry 1). The structure of **3a** was verified by ^{1}H and ^{13}C NMR and mass spectroscopy, as well as X-ray diffraction analysis (see Supporting Information). Further screening of solvents revealed that the yield could be dramatically improved when THF was used in the reaction (98% yield, Table 1, entry 7). Inferior results were displayed when other solvents were used. Other metal salts such as $Zn(OTf)_2$, $Yb(OTf)_3$, and $In(OTf)_3$ were also tried in the reaction, and silver triflate was demonstrated to be the best choice (Table 1, entries 8−16). Similar result was observed when the catalytic amount of silver triflate reduced to 5 mol % (96% yield, Table 1, entry 17). Gratifyingly, 1 mol% of AgOTf was found to be sufficient for catalysis of 2,4-dihydro-1*H*-benzo[*d*][1,3]thiazine synthesis although prolonged reaction time was needed for completion with slightly lower yield (36 h, 90% yield). The result also provides evidence that there is no deactivation or

Scheme 1

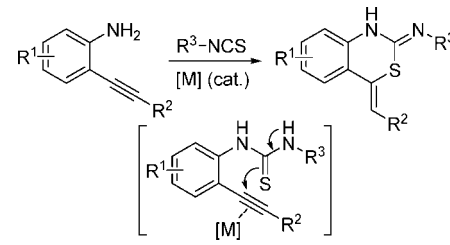

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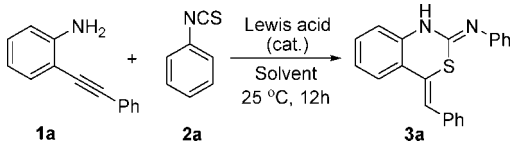
Table 1. Conditions Screening for the Reaction of 2-Alkynylbenzenamine **1a** with Phenyl Isothiocyanate **2a** Catalyzed by Lewis Acid[a]



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

entry	Lewis acid	solvent	yield (%)[b]
1	AgOTf (10 mol %)	$(CH_2Cl)_2$	66
2	AgOTf (10 mol %)	CH_2Cl_2	44
3	AgOTf (10 mol %)	MeCN	35
4	AgOTf (10 mol %)	toluene	59
5	AgOTf (10 mol %)	EtOH	55
6	AgOTf (10 mol %)	DMF	78
7	AgOTf (10 mol %)	THF	98
8	CuI (10 mol %)	THF	78
9	$FeCl_3$ (10 mol %)	THF	18
10	$Zn(OTf)_2$ (10 mol %)	THF	68
11	$Yb(OTf)_3$ (10 mol %)	THF	37
12	$Dy(OTf)_3$ (10 mol %)	THF	31
13	$In(OTf)_3$ (10 mol %)	THF	57
14	$Pd(OAc)_2$ (10 mol %)	THF	60
15	$PdCl_2$ (10 mol %)	THF	33
16	$PdCl_2(PhCN)_2$ (10 mol %)	THF	37
17	AgOTf (5 mol %)	THF	96
18	AgOTf (1 mol %)	THF	90

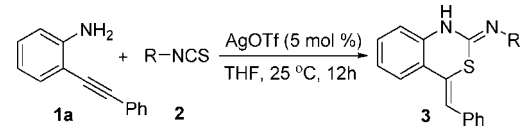
[a] Reaction conditions: 2-alkynylbenzenamine **1a** (0.50 mmol), phenyl isothiocyanate **2a** (1.0 mmol, 2.0 equiv), Lewis acid (cat.), solvent (0.5 mL), 25 °C, 12 h. [b] Isolated yield based on 2-alkynylbenzenamine **1a**.

inhibition of silver catalyst, which is of interest considering that the reactants and/or the intermediate might act as a Lewis base.

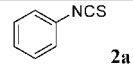
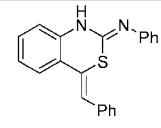
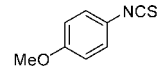
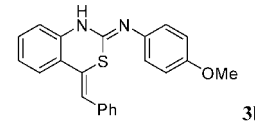
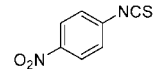
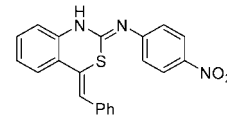
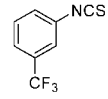
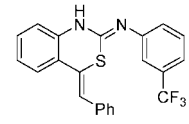
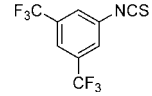
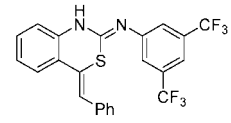
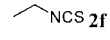
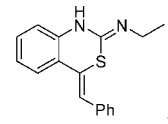
We then investigated the reaction scope of this silver triflate catalytic system and its tolerance of functional groups in the case of other 2-alkynylbenzenamines **1** and isothiocycanates **2** under the optimized conditions [AgOTf (5 mol %), THF, 25 °C] (Tables 2 and 3). We rapidly noticed the broad field of application of the process and its remarkable functional group compatibility on both reagents. With respect to the aryl or alkyl isothiocycanates, the expected 2,4-dihydro-1*H*-benzo[*d*][1,3]thiazines resulting from reactions of 2-alkynylbenzenamine **1a** were obtained and isolated in good to excellent yields (Table 2). We found that the conditions have proven to be useful for various isothiocycanates. As expected, both electron-rich and electron-poor aryl isothiocycanates are suitable partners in this process because of the high electrophilicity of isothiocycanate. For instance, 2-alkynylbenzenamine **1a** reacted with 4-methoxyphenyl isothiocycanate **2b** leading to the desired product **3b** in 83% yield (Table 2, entry 2), while a 95% yield of product **3c** was obtained when 4-nitrophenyl isothiocycanate **2c** was employed in the reaction (Table 2, entry 3). In addition to aryl isothiocycanates, reactions of alkyl isothiocycanates such as **2f** also proceeded smoothly to give rise to the corresponding products **3f** in moderate yield (55% yield, Table 2, entry 6).

In a second set of experiments, the scope of the process with respect to 2-alkynylbenzenamine substituted with electron-rich and -poor substituents was investigated. All the expected products were generated under our standard experimental conditions, whatever the nature of the substituents. For example, reaction of 2-alkynylbenzenamine **1b** with 3,5-ditrifluoromethylphenyl isothiocycanate **2e** afforded the desired product **3i** in 96% yield (Table

Table 2. Reactions of 2-Alkynylbenzenamine **1a** with Various Isothiocyanates **2** Catalyzed by Silver Triflate

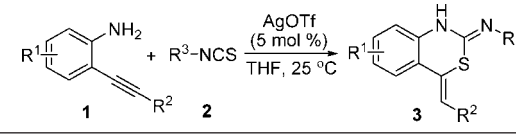


1a **2** **3**

entry	isothiocyanate **2**	product **3**	yield (%)[a]
1	 **2a**	 **3a**	96
2	 **2b**	 **3b**	83
3	 **2c**	 **3c**	95
4	 **2d**	 **3d**	94
5	 **2e**	 **3e**	92
6	 **2f**	 **3f**	55

[a] Isolated yield based on 2-alkynylbenzenamine **1**.

Table 3. Reaction of 2-Alkynylbenzenamine**1** with Isothio-cyanate **2** Catalyzed by Silver Triflate



1 **2** **3**

entry	R^1/R^2	R^3	yield (%)[a]
1	H/*p*-$MeOC_6H_4$ (**1b**)	Ph (**2a**)	87 (**3g**)
2	H/*p*-$MeOC_6H_4$ (**1b**)	*p*-$MeOC_6H_4$ (**2b**)	69 (**3h**)
3	H/*p*-$MeOC_6H_4$ (**1b**)	3,5-$(CF_3)_2C_6H_3$ (**2e**)	96 (**3i**)
4	H/*n*-Bu (**1c**)	Ph (**2a**)	87 (**3j**)
5	H/*n*-Bu (**1c**)	*p*-$MeOC_6H_4$ (**2b**)	76 (**3k**)
6	H/*n*-Bu (**1c**)	*m*-$CF_3C_6H_4$ (**2d**)	73 (**3l**)
7	H/cyclopropyl (**1d**)	Ph (**2a**)	70 (**3m**)
8	H/cyclopropyl (**1d**)	*p*-$MeOC_6H_4$ (**2b**)	68 (**3n**)
9	H/cyclopropyl (**1d**)	*m*-$CF_3C_6H_4$ (**2d**)	89 (**3o**)
10	CH_3/Ph (**1e**)	Ph (**2a**)	98 (**3p**)
11	CH_3/Ph (**1e**)	*p*-$MeOC_6H_4$ (**2b**)	78 (**3q**)
12	CH_3/Ph (**1e**)	*m*-$CF_3C_6H_4$ (**2d**)	92 (**3r**)
13	CH_3/Ph (**1e**)	Et (**2f**)	50 (**3s**)
14	CF_3/Ph (**1f**)	Ph (**2a**)	72 (**3t**)
15	CF_3/Ph (**1f**)	*m*-$CF_3C_6H_4$ (**2d**)	95 (**3u**)

[a] Isolated yield based on 2-alkynylbenzenamine **1**.

3, entry 3). When R^2 was changed to *n*-butyl or cyclopropyl, the reactions also occurred smoothly to generate the corresponding products in good yields (Table 3, entries 4−9). 2-Alkynylbenzenamines with substituents on aromatic ring were also tried and similar results were obtained (Table 3, entries 10−15). For instance, almost quantitative yield of product **3p** was isolated in the reaction of 2-alkynylbenzenamine **1e** with phenyl isothiocyanate **2a** (98% yield, Table 3, entry 10).

Conclusion

In summary, we have described a novel and efficient method for the synthesis of 2,4-dihydro-1*H*-benzo[*d*]-[1,3]thiazine derivatives via AgOTf-catalyzed tandem addition-cyclization reactions of 2-alkynylbenzenamines with isothiocyanates. The presented tandem addition-cyclization reaction represented a facile route for generation of *N*-heterocycles. Construction of small library and biological screening of these small molecules are under investigation in our laboratory, and the results will be reported in due course.

Experimental Section

All reactions were performed in test tubes under nitrogen atmosphere. Flash column chromatography was performed using silica gel (60 Å pore size, 32−63 μm, standard grade). Analytical thin-layer chromatography was performed using glass plates precoated with 0.25 mm 230−400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light. Organic solutions were concentrated on rotary evaporators at ~20 Torr (house vacuum) at 25−35 °C. Commercial reagents and solvents were used as received.

General Procedure for Reaction of 2-Alkynylbenzenamine 1 with Isothiocyanate 2 Catalyzed by Silver Triflate. A solution of 2-(1-alkynyl)aniline **1**[7] (0.50 mmol), isothiocyanate **2** (1.0 mmol, 2.0 equiv), and AgOTf (0.025 mmol, 5 mol %) in THF (0.5 mL) was stirred at room temperature overnight. After completion of reaction as indicated by TLC, the solvent was evaporated, and the residue was quenched with water (10 mL), extracted with EtOAc (2 × 10 mL), and dried by anhydrate Na_2SO_4. Evaporation of the solvent, followed by purification on silica gel, provided the corresponding product **3**. (For details, please see Supporting Information.)

4-Benzylidene-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)-benzenamine 3a: yield 96%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (t, J = 7.3 Hz, 1H), 7.17 (s, 1H), 7.19 (dd, J = 1.5, 7.8 Hz, 1H), 7.27−7.40 (m, 5H), 7.41−7.45 (m, 4H), 7.53−7.58 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 120.2, 121.7, 123.5, 124.8, 124.9, 125.9, 126.6, 127.1, 127.7, 128.2, 128.9, 129.3, 129.6, 135.6, 139.9, 143.2, 147.6; MS (EI) *m*/*z* 328 (M^+); elemental analysis calcd (%) for $C_{21}H_{16}N_2S$ C 76.80, H 4.91, N 8.53; found C 76.64, H 4.92, N 8.62.

4-Benzylidene-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)-4-methoxybenzenamine 3b: yield 83%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, 3H), 6.85 (d, J = 8.8 Hz, 2H), 7.12−7.20 (m, 3H), 7.28−7.42 (m, 8H), 7.53 (dd, J = 1.5, 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.5, 114.1, 121.6, 122.7, 124.4, 124.7, 125.5, 126.7, 126.8, 128.2, 129.3, 129.6, 132.9, 135.7, 143.2, 148.6, 156.1; MS (EI) *m*/*z* 358 (M^+); elemental analysis calcd (%) for $C_{22}H_{18}N_2OS$ C 73.71, H 5.06, N 7.82; found C 73.75, H 5.19, N 7.63.

4-Benzylidene-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)-4-nitrobenzenamine 3c: yield 95%; ^{1}H NMR (400 MHz, DMSO) δ 7.18−7.50 (m, 10H), 7.65 (d, J = 7.3 Hz, 1H), 8.02 (d, J = 8.0 Hz, 2H), 8.13 (d, J = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, DMSO) δ 119.1, 119.2, 121.3, 125.3, 125.4, 125.8, 126.4, 127.3, 128.3, 128.8, 129.7, 130.4, 135.8, 141.7, 142.9, 146.7, 147.3; MS (EI) *m*/*z* 373 (M^+); elemental analysis calcd (%) for $C_{21}H_{15}N_3O_2S$ C 67.54, H 4.05, N 11.25; found C 67.25, H 4.10, N 10.92.

4-Benzylidene-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)-3-(trifluoromethyl)benzenamine 3d: yield 94%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (br, 1H), 7.16 (s, 1H), 7.19 (dd, J = 2.0, 7.8 Hz, 2H), 7.28−7.44 (m, 8H), 7.53 (dd, J = 1.5, 9.3 Hz, 1H), 7.57 (d, J = 8.3 Hz, 1H), 7.90 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 117.1, 119.8, 119.9, 121.8, 123.2, 123.9 (q, $^1J_{CF}$ = 270.8 Hz), 124.9, 125.1, 125.9, 127.6, 127.8, 128.2, 129.3, 129.4, 129.7, 131.3 (q, $^2J_{CF}$ = 32.4 Hz), 135.4, 141.2, 142.1, 148.0; MS (EI) *m*/*z* 396 (M^+); elemental analysis calcd (%) for $C_{22}H_{15}F_3N_2S$ C 66.65, H 3.81, N 7.07; found C 66.27, H 3.74, N 7.03.

4-Benzylidene-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)-3,5-bis(trifluoromethyl)benzenamine 3e: yield 92%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 (br, 1H), 7.14 (d, J = 7.8 Hz, 1H), 7.17 (s, 1H), 7.20 (t, J = 7.8 Hz, 1H), 7.30−7.43 (m, 6H), 7.53 (s, 1H), 7.54 (d, J = 7.8 Hz, 1H), 7.96 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 116.5, 120.2, 121.9, 123.2 (q, $^1J_{CF}$ = 270.8 Hz), 125.0, 125.1, 128.0, 128.3, 128.4, 129.3, 129.9, 132.1 (q, $^2J_{CF}$ = 32.4 Hz), 135.2, 141.1, 142.8, 148.4; MS (EI) *m*/*z* 464 (M^+); elemental analysis calcd (%) for $C_{23}H_{14}F_6N_2S$ C 59.48, H 3.04, N 6.03; found C 59.22, H 3.21, N 5.94.

4-Benzylidene-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)ethanamine 3f: yield 55%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (t, J = 7.3 Hz, 3H), 3.49 (q, J = 7.3 Hz, 2H), 4.43 (br, 1H), 7.09 (t, J = 7.3 Hz, 1H), 7.11 (s, 1H), 7.17 (d, J = 7.3 Hz, 1H), 7.27−7.33 (m, 2H), 7.37−7.42 (m, 4H), 7.50 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 37.2, 121.5, 123.8, 124.7, 126.0, 126.1, 127.2, 127.4, 128.1, 129.3, 129.6, 135.9, 144.6, 150.9; Ms (EI) *m*/*z* 280 (M^+); elemental analysis calcd (%) for $C_{17}H_{16}N_2S$ C 72.82, H 5.75, N 9.99; Found C 72.45, H 5.60, N 9.87.

4-(4-Methoxybenzylidene)-1*H*-benzo[*d*][1,3]thiazin-2-(4H)-ylidene)benzenamine 3g: yield 87%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.81 (s, 3H), 6.92 (d, J = 8.8 Hz, 2H), 7.05 (t, J = 7.3 Hz, 1H), 7.07 (s, 1H), 7.13 (t, J = 7.3 Hz, 1H), 7.21 (d, J = 7.3 Hz, 1H), 7.27−7.32 (m, 3H), 7.36 (d, J = 8.3 Hz, 2H), 7.46−7.53 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2, 113.6, 120.4, 122.1, 123.4, 124.3, 124.6, 124.8, 125.3, 126.9, 128.4, 128.9, 129.3, 130.8, 140.2, 142.8, 148.0, 159.0; MS (EI) *m*/*z* 358 (M^+); elemental analysis calcd (%) for $C_{22}H_{18}N_2OS$ C 73.71, H 5.06, N 7.82; Found C 73.40, H 4.99, N 7.51.

4-(4-Methoxybenzylidene)-1*H*-benzo[*d*][1,3]thiazin-2-(4*H*)-ylidene)-4-methoxybenzenamine 3h: yield 69%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, 3H), 3.84 (s, 3H), 6.86

(d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H), 7.08 (s, 1H), 7.13 (t, J = 7.3 Hz, 1H), 7.18 (d, J = 7.3 Hz, 1H), 7.31(t, J = 7.8 Hz, 1H), 7.37 (d, J = 8.8 Hz, 2H), 7.41 (d, J = 8.8 Hz, 2H), 7.50 (d, J = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.3, 55.5, 113.6, 114.1, 122.1, 122.7, 124.4, 124.7, 125.3, 126.7, 128.4, 129.3, 130.8, 133.0, 143.1, 148.7, 156.1, 159.0; MS (EI) *m*/*z* 388 (M^+); elemental analysis calcd (%) for $C_{23}H_{20}N_2O_2S$ C 71.11, H 5.19, N 7.21; found C 70.78, H 4.93, N 6.97.

4-(4-Methoxybenzylidene)-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)-3,5-bis(trifluoromethyl)benzenamine 3i: yield 96%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 (d, J = 8.3 Hz, 2H), 7.08−7.14 (m, 3H), 7.18 (t, J = 7.3 Hz, 1H), 7.31−7.34 (m, 3H), 7.51 (d, J = 7.8 Hz, 1H), 7.53 (s, 1H), 7.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.3, 113.7, 116.4, 120.3, 122.3, 122.7, 123.0 (q, $^1J_{CF}$ = 271.7 Hz), 123.8, 125.0, 125.2, 127.2, 127.9, 128.3, 129.6, 130.8, 132.1 (q, $^2J_{CF}$ = 33.3 Hz), 140.7, 143.2, 148.8, 159.3; MS (EI) *m*/*z* 494 (M^+); elemental analysis calcd (%) for $C_{24}H_{16}F_6N_2OS$ C 58.30, H 3.26, N 5.67; found C 58.30, H 3.38, N 5.56.

4-Pentylidene-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)-benzenamine 3j: yield 87%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, J = 7.3 Hz, 3H), 1.31−1.49 (m, 4H), 2.23 (q, J = 7.3 Hz, 2H), 6.10 (t, J = 7.3 Hz, 1H), 7.02−7.11 (m, 3H), 7.20 (dt, J = 1.5, 7.3 Hz, 1H), 7.29−7.36 (m, 3H), 7.41 (d, J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.2, 28.8, 31.1, 121.2, 121.5, 123.6, 124.0, 124.1, 124.7, 128.6, 128.9, 129.0, 129.2, 141.7, 141.8, 149.9; MS (EI) *m*/*z* 308 (M^+); elemental analysis calcd (%) for $C_{19}H_{20}N_2S$ C 73.99, H 6.54, N 9.08; found C 73.82, H 6.55, N 8.76.

4-Methoxy-*N*-((*Z*)-4-pentylidene-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)benzenamine 3k: yield 76%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, J = 7.3 Hz, 3H), 1.31−1.47 (m, 4H), 2.20 (q, J = 7.3 Hz, 2H), 3.79 (s, 3H), 6.07 (t, J = 7.3 Hz, 1H), 6.93 (d, J = 8.8 Hz, 1H), 6.86 (d, J = 8.8 Hz, 2H), 6.96−7.02 (m, 2H), 7.17 (t, J = 7.8 Hz, 1H), 7.27 (d, J = 8.8 Hz, 2H), 7.35(d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.2, 28.7, 31.1, 55.4, 114.1, 121.3, 123.2, 123.6, 123.7, 124.0, 124.9, 128.2, 128.9, 134.7, 141.7, 151.3, 156.3; MS (EI) *m*/*z* 338 (M^+); elemental analysis calcd (%) for $C_{20}H_{22}N_2OS$ C 70.97, H 6.55, N 8.28; found C 71.22, H 6.42, N 8.21.

4-Pentylidene-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)-3-(trifluoromethyl)benzenamine 3l: yield: 73%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, J = 7.3 Hz, 3H), 1.31−1.49 (m, 4H), 2.23 (q, J = 7.3 Hz, 2H), 6.12 (t, J = 7.3 Hz, 2H), 6.94 (d, J = 7.8 Hz, 1H), 7.05 (t, J = 7.8 Hz, 1H), 7.19 (dt, J = 1.5, 7.8 Hz, 1H), 7.33 (d, J = 7.8 Hz, 1H), 7.36 (d, J = 7.8 Hz, 1H), 7.42 (t, J = 8.0 Hz, 1H), 7.49 (d, J = 7.8 Hz, 1H), 7.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 22.2, 28.8, 31.0, 118.2, 120.0, 121.5, 122.5, 124.0 (q, $^1J_{CF}$ = 270.8 Hz), 124.2, 124.3, 124.4, 129.1, 129.4, 131.3 (q, $^2J_{CF}$ = 32.4 Hz), 140.4, 143.5, 150.5; MS (EI) *m*/*z* 409 (M^+); elemental analysis calcd (%) for $C_{20}H_{19}F_3N_2S$ C 63.81, H 5.09, N 7.44; found C 64.20, H 5.19, N 7.14.

4-(Cyclopropylmethylene)-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)benzenamine 3m: yield 70%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.52−0.57 (m, 2H), 0.88−0.93 (m, 2H), 1.67−1.76 (m, 1H), 5.50 (d, J = 9.8 Hz, 1H), 7.01−7.11 (m, 3H), 7.22 (t, J = 7.3 Hz, 1H), 7.28 (d, J = 7.3 Hz, 1H), 7.33 (t, J = 7.8 Hz, 2H), 7.45 (d, J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.8, 11.9, 121.0, 121.6, 122.5, 123.6, 123.8, 124.1, 128.8, 128.9, 132.6, 141.5, 141.7, 149.3; MS (EI) *m*/*z* 292 (M^+); elemental analysis calcd (%) for $C_{18}H_{16}N_2S$ C 73.94, H 5.52, N 9.58; found: C 73.62, H 5.37, N 9.33.

4-(Cyclopropylmethylene)-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)-4-methoxybenzenamine 3n: yield 68%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.50−0.54 (m, 2H), 0.85−0.90 (m, 2H), 1.63−1.73 (m, 1H), 3.79 (s, 3H), 5.46 (d, J = 9.8 Hz, 1H), 6.86 (d, J = 8.8 Hz, 2H), 6.93−7.00 (m, 2H), 7.14 (dt, J = 1.0, 7.8 Hz, 1H), 7.23−7.29 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.7, 11.9, 55.4, 114.0, 121.4, 122.6, 122.9, 123.5, 123.7, 123.8, 128.7, 132.2, 134.9, 141.3, 151.4, 156.3; MS (EI) *m*/*z* 322 (M^+); elemental analysis calcd (%) for $C_{19}H_{18}N_2OS$ C 70.78, H 5.63, N 8.69; found C 70.48, H 5.81, N 8.45.

4-(Cyclopropylmethylene)-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)-3-(trifluoromethyl)benzenamine 3o: yield 89%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.52−0.56 (m, 2H), 0.88−0.92 (m, 2H), 1.63−1.72 (m, 1H), 5.49 (d, J = 9.3 Hz, 1H), 6.88 (d, J = 7.8 Hz, 1H), 7.00 (dt, J = 1.2, 7.3 Hz, 1H), 7.15 (dt, J = 1.0, 7.3 Hz, 1H), 7.26 (dd, J = 1.5, 7.8 Hz, 1H), 7.33 (d, J = 7.8 Hz, 1H), 7.39−7.48 (m, 2H), 7.67 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.8, 11.9, 118.4, 120.1, 121.6, 121.7, 121.9, 124.0, 124.1 (q, $^1J_{CF}$ = 271.7 Hz), 124.7, 128.7, 129.4, 131.3 (q, $^2J_{CF}$ = 32.4 Hz), 133.4, 139.8, 144.0, 150.9; MS (EI) *m*/*z* 360 (M^+); elemental analysis calcd (%) for $C_{19}H_{15}F_3N_2S$ C 63.32, H 4.20, N 7.77; found C 63.53, H 4.50, N 8.10.

4-Benzylidene-6-methyl-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)benzenamine 3p: yield 98%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 7.04 (t, J = 7.3 Hz, 1H), 7.13−7.17 (m, 3H), 7.27−7.33 (m, 3H), 7.35 (s, 1H), 7.38−7.43 (m, 4H), 7.53 (d, J = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 119.5, 120.8, 122.8, 124.5, 125.3, 126.1, 126.3, 127.0, 127.6, 128.4, 128.8, 130.0, 133.9, 135.2, 139.4, 140.4, 146.4; MS (EI) *m*/*z* 342 (M^+); elemental analysis calcd (%) for $C_{21}H_{16}N_2S$ C 77.16, H 5.30, N 8.18; found C 76.97, H 5.10, N 8.31.

4-Benzylidene-6-methyl-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)-4-methoxybenzenamine 3q: yield 78%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 3.77 (s, 3H), 6.84 (d, J = 8.8 Hz, 2H), 7.08−7.15 (m, 3H), 7.28 (t, J = 6.8 Hz, 1H), 7.33 (s, 1H), 7.36−7.43 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 55.4, 114.1, 121.2, 122.6, 125.0, 125.5, 126.4, 126.9, 127.5, 128.1, 129.3, 130.5, 132.9, 134.0, 135.8, 141.0, 148.0, 156.0; MS (EI) *m*/*z* 372 (M^+); elemental analysis calcd (%) for $C_{23}H_{20}N_2OS$: C 74.16, H 5.41, N 7.52; found: C 73.90, H 5.18, N 7.45.

4-Benzylidene-6-methyl-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)-3-(trifluoromethyl)benzenamine 3r: yield 92%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 6.75 (br, 1H), 7.10 (d, J = 8.3 Hz, 1H), 7.13−7.17 (m, 2H), 7.25−7.33 (m, 3H), 7.34 (s, 1H), 7.36−7.43 (m, 4H), 7.57 (d, J = 7.8 Hz, 1H), 7.90 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 116.9, 119.7, 121.4, 123.0, 123.9 (q, $^1J_{CF}$ = 270.2 Hz), 125.1, 125.2, 126.2, 127.2, 127.7, 128.2, 129.3, 129.4, 130.6, 131.2 (q, $^2J_{CF}$ = 32.4 Hz), 134.8, 135.6, 140.0, 141.1, 147.2; MS

(EI) *m*/*z* 410 (M^+); elemental analysis calcd (%) for $C_{23}H_{17}F_3N_2S$ C 67.30, H 4.17, N 6.82; found C 67.58, H 4.31, N 6.62.

4-Benzylidene-6-methyl-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)ethanamine 3s: yield 50%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (t, J = 7.3 Hz, 3H), 2.36 (s, 3H), 3.48 (q, J = 6.8 Hz, 2H), 4.38 (br, 1H), 7.07−7.14 (m, 3H), 7.26−7.33 (m, 2H), 7.36−7.42 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 21.0, 37.2, 121.1, 124.9, 125.7, 125.9, 127.3, 127.4, 128.1, 129.3, 130.4, 133.2, 135.9, 142.2, 150.3; MS (EI) *m*/*z* 294 (M^+); elemental analysis calcd (%) for $C_{18}H_{18}N_2S$ C 73.43, H 6.16, N 9.51; found: C 73.17, H 6.03, N 9.34.

4-Benzylidene-6-(trifluoromethyl)-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)benzenamine 3t: yield 72%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (t, J = 7.3 Hz, 1H), 7.19 (s, 1H), 7.26−7.36 (m, 4H), 7.40−7.43 (m, 4H), 7.51−7.57 (m, 3H), 7.75 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 120.7, 122.1, 122.2, 124.1, 124.2 (q, $^1J_{CF}$ = 270.0 Hz), 125.1, 126.1, 126.2, 126.4 (q, $^2J_{CF}$ = 32.4 Hz), 128.1, 128.3, 128.8, 129.0, 129.4, 135.1, 139.2, 146.2, 149.7; MS (EI) *m*/*z* 396 (M^+); elemental analysis calcd (%) for $C_{22}H_{15}F_3N_2S$ C 66.65, H 3.81, N 7.07; found C 66.32, H 3.73, N 6.94.

4-Benzylidene-6-(trifluoromethyl)-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-ylidene)-3-(trifluoromethyl)benzenamine 3u: yield 95%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (br, 1H), 7.20 (s, 1H), 7.26 (d, J = 8.3 Hz, 1H), 7.31−7.44 (m, 7H), 7.56 (d, J = 8.3 Hz, 1H), 7.61 (d, J = 7.3 Hz, 1H), 7.76 (s, 1H), 7.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 117.3, 120.4, 122.2, 122.3, 123.4, 123.8 (q, $^1J_{CF}$ = 270.2 Hz), 124.1 (q, $^1J_{CF}$ = 270.5 Hz), 124.4, 125.7, 126.2, 126.3, 126.9 (q, $^2J_{CF}$ = 32.4 Hz), 128.3, 129.4, 129.5, 131.4 (q, $^2J_{CF}$ = 32.4 Hz), 134.9, 140.2, 145.4, 149.6; MS *m*/*z* 465.1 (M^+ + 1); elemental analysis calcd (%) for $C_{23}H_{14}F_6N_2S$ C 59.48, H 3.04, N 6.03; found C 59.10, H 3.05, N 5.73.

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Supporting Information Available. Experimental procedures, characterization data including X-ray diffraction analysis data of compound **3a**, and copies of ^{1}H and ^{13}C NMR of compound **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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