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N-Heterocyclic Carbene-Catalyzed *in situ* Activation of Alkynyl Acids for C-S Bond Formation: Access to Imidazo[2,1-*b*][1,3]thiazinones

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Abstract. Alkynyl acids are first utilized as alkynyl acylazolium precursors through an *in situ* activation strategy for the efficient construction of carbon-sulfur bond in a formal [3+3] annulation. This protocol offers a direct and rapid pathway for the synthesis of imidazo[2,1-*b*][1,3]thiazinone skeleton, a useful heterocyclic class frequently found in many bioactive compounds. This reaction also has the advantages of scalability, readily available materials, and simple manipulation in open air.

Keywords: carbene; alkynyl acid; in situ activation; C-S bond formation; heterocyclic compounds

Introduction

Over the last decade, N-heterocyclic carbenes (NHCs) have been used as efficient organocatalysts to enable numerous unconventional transformations due to their unique reactivity. Among these transformations, nucleophilic NHCs can combine with different carbonyl compounds to generate several key NHC-bound intermediates like homoenolates, enolates, alkenyl acylazoliums and vinyl enolates that have been extensively studied and applied in diverse annulation reactions to access a variety of heterocyclic compounds (Figure 1). [1]

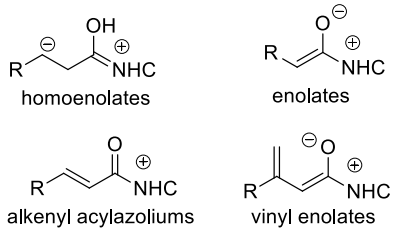
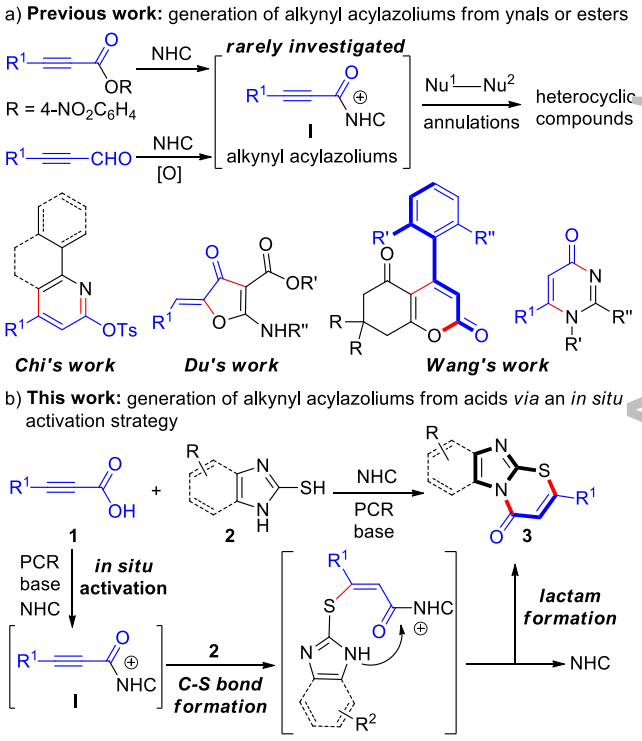


Figure 1. Extensively studied NHC-bound intermediates.

However, as another important type of NHC-bound intermediate, alkynyl acylazoliums **I** were rarely investigated,[2] and limited annulation reactions with diverse binucleophiles were documented (Scheme 1a).[3] In 2017, Chi's group[3a] and our group[3b]independently applied *p*-nitrophenyl alkynyl esters as the alkynyl acylazolium precursors to undergo two different NHC-catalyzed annulations, affording a series of functionalized pyridines and (*Z*) 5-amino-3-furanones, respectively. Very recently, Wang and co-workers [3c, 3d]reported two formal [3+3]



Scheme 1. Generation and reactions of alkynyl acylazoliums.

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annulations of alkynyl acylazoliums **I** derived from ynals under oxidative NHC conditions, giving rise to axially chiral α-pyrone-aryls and trisubstituted pyrimidin-4-ones, respectively. Therefore, it is still in demand to further investigate the reactivity of alkynyl acylazoliums **I** and enrich their applications in the organic synthesis.

In the field of NHC organocatalysis, compared to frequently used ester and aldehyde substrates, carboxylic acids are more readily available and easier to handle. In recent years, saturated[4]and α,β-unsaturated alkenyl[5]carboxylic acids have been applied to generate some important NHC-bound intermediates such as enolates, alkenyl acylazoliums and vinyl enolates through an *in situ* activation strategy. Therefore, we reasoned that *in situ* activation of alkynyl acids **1** with NHC catalysis might afford alkynyl acylazoliums **I** in a direct manner (Scheme 1b). The construction of carbon-sulfur (C-S) bond has been one of the research interests in organic synthesis owing to wide prevalence of C-S bond in many biologically active molecules.[6] However, there are limited examples of C-S bond construction in the field of NHC catalysis.[7] We envisioned that the combination of alkynyl acylazoliums **I** with 2-mercaptobenzimidazoles or 2-mercaptoimidazoles **2** might undergo a Michael addition to construct the C-S bond followed by lactam formation to afford a series of imidazo[2,1-*b*][1,3]thiazinones **3** (Scheme 1b). Notably, the imidazo[2,1-*b*][1,3]thiazinone skeleton is an interesting structure widely found in organic compounds possessing important pharmacological activities (Figure 2), [8]and thus, the synthesis of this skeleton has evoked much interest of chemists. [9] Herein, we report an efficient and rapid pathway to access functionalized imidazo [2,1-*b*][1,3]thiazinones from simple and readily available starting materials with NHC catalysis.

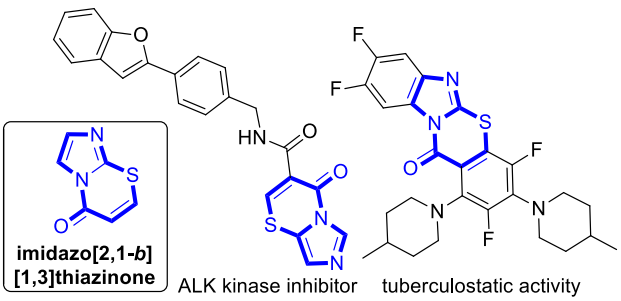
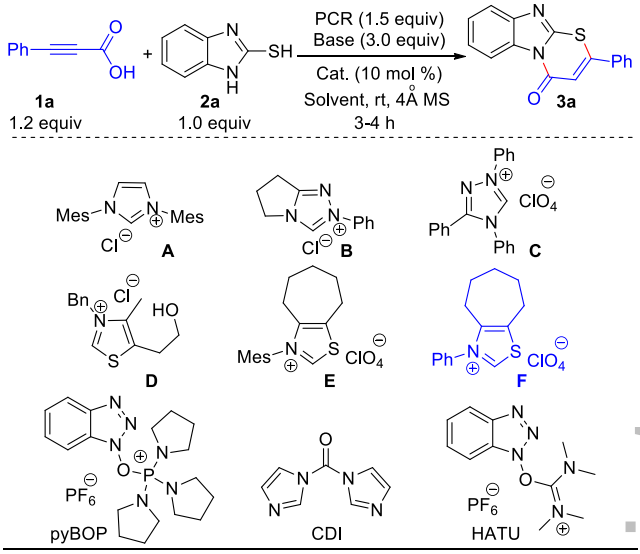


Figure 2. Representative bioactive compounds with the imidazo[2,1-*b*][1,3]thiazinone skeleton.

Results and Discussion

Commercially available 3-phenylpropiolic acid **1a** and 2-mercaptobenzimidazole **2a** were used as the model substrates for our initial attempt (Table 1). The reaction between **1a** and **2a** was carried out in the presence of a series of NHC precursors **A-F** using pyBOP as the peptide coupling reagent (PCR) and DIPEA as a base under N_2 atmosphere. It was found

Table 1. Optimization of the reaction conditions[a]



Entry	Cat.	PCR	Base	Solvent	Yield [%][b]
1	A	pyBOP	DIPEA	PhMe	63
2	B	pyBOP	DIPEA	PhMe	41
3	C	pyBOP	DIPEA	PhMe	65
4	D	pyBOP	DIPEA	PhMe	41
5	E	pyBOP	DIPEA	PhMe	82
6	F	pyBOP	DIPEA	PhMe	83
7	none	pyBOP	DIPEA	PhMe	0
8	F	pyBOP	DBU	PhMe	36
9	F	pyBOP	Et_3N	PhMe	69
10	F	pyBOP	Cs_2CO_3	PhMe	54
11	F	pyBOP	DIPEA	THF	57
12	F	pyBOP	DIPEA	DCM	80
13	F	pyBOP	DIPEA	CH_3CN	92
14	F	CDI	DIPEA	CH_3CN	12
15	F	HATU	DIPEA	CH_3CN	82
16[c]	F	pyBOP	DIPEA	CH_3CN	92

[a]All reactions were performed on a 0.15 mmol scale with 1.2 equiv of **1a**, 1.0 equiv of **2a**, 1.5 equiv of a PCR, 3.0 equiv of a base, 10 mol % of a NHC precursor, 150 mg of 4Å MS (molecular sieves), in an anhydrous solvent (3 mL) at rt for 3-4 h under N_2.
[b]Isolated yields based on **2a**.
[c]The reaction was carried out in open air. Mes = 2,4,6-$(CH_3)_3C_6H_2$.

that the reaction with NHC catalysis could afford the desired product **3a** in moderate to good yields (entries 1-6), while the reaction did not work in the absence of an NHC precursor (entry 7). Further examination of the bases and solvents in the presence of catalyst **F** (entries 8-13) revealed that DIPEA and CH_3CN are the

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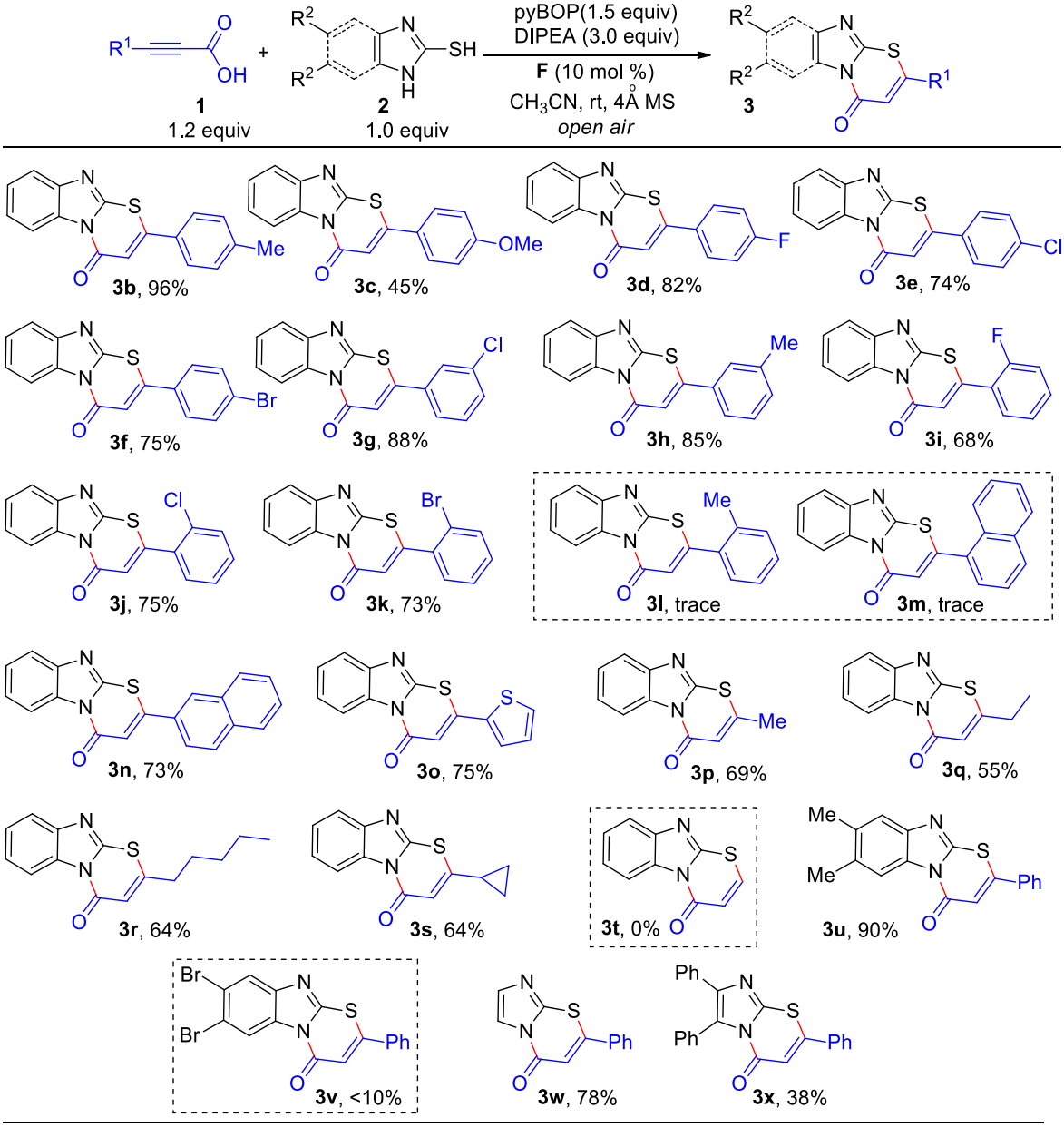
Table 2. The scope of the reaction between symmetric 2-mercaptobenzimidazoles or 2-mercaptoimidazoles **2** and diverse alkynyl acids **1** [a]



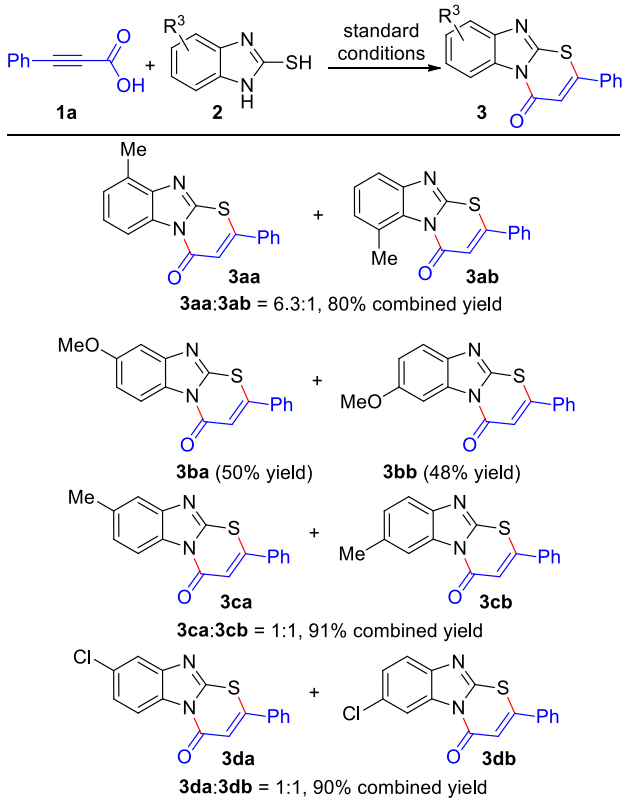
[a]All reactions were performed on a 0.15 mmol scale with 1.2 equiv of **1**, 1.0 equiv of **2**, 1.5 equiv of pyBOP, 3.0 equiv of DIPEA, 10 mol % of **F**, 150 mg of 4Å MS, in anhydrous CH_3CN (3 mL) at rt for 3-4 h in open air. All yields are isolated yields based on **2**.

optimal base and solvent, respectively, and the desired product **3a** was obtained in 92% yield (entry 13). We also tested other PCRs such as CDI and HATU, but resulting in decreased yields (entries 14-15). We were happy to find that the reaction carried out in open air without nitrogen protection had no influence on the reaction yield (entry 16). Therefore, the optimal reaction conditions were established as that in entry 16 for further scope exploration.

With the optimal reaction conditions in hand, we moved our attention to explore the scope of this reaction (Table 2). Initially, a wide range of 3-arylpropiolic acids **1** were examined. The reaction could accommodate various 3-(substituted phenyl) propiolic acids with diverse substituents at different positions on the phenyl ring, affording the corresponding products **3b-k** in moderate to high yields. However, 3-(2-methylphenyl)propiolic acid was not tolerated probably due to the steric effect of the more hindered 2-methyl group. Similarly, the more hindered 3-(naphthalen-1-yl)propiolic acid was also unsuitable to this protocol, but the less hindered 3-(naphthalen-2-yl)propiolic acid as well as 3-(thiophen-2-yl)propiolic acid were well tolerated under the optimal reaction conditions, affording products **3n** and **3o**, respectively, in moderate yields. Then, 3-alkyl-substituted alkynyl acids were tested. It was gratifying

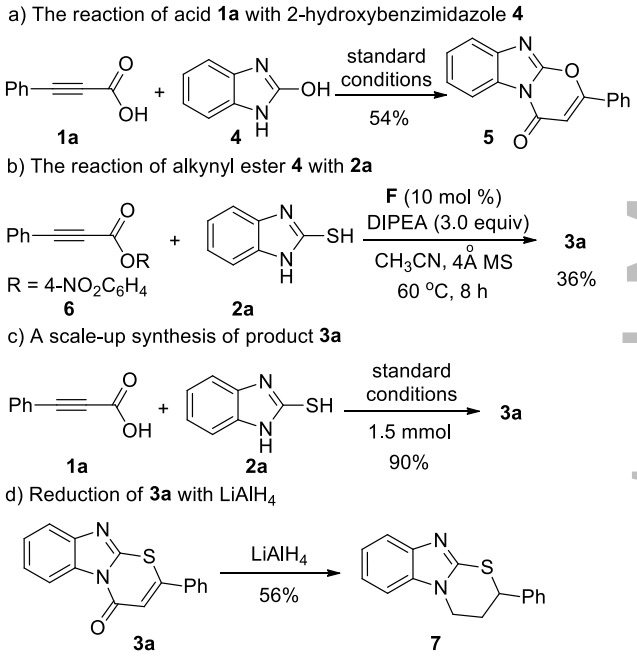
that the size and length of the alkyl groups had little impact on the reaction results and the desired products **3p-s** were obtained in moderate yields. However, an aryl or an alkyl group at the 3-position of the acids proved essential to this protocol since **3t** was not formed when propiolic acid was used as the substrate. Finally, two 4,5-disubstituted 2-mercaptobenzimidazoles were used to further explore the generality of this reaction. The electronic nature of the substituents seemed to have great influence on the reaction results. The reaction of 5,6-dimethyl-2-mercaptobenzimidazole gave product **3u** in a high yield, while substrate 5,6-dibromo-2-mercaptobenzimidazole was unsuitable to this protocol. Moreover, the reactions of two 2-mercaptoimidazoles with **1a** were examined. As a result, the reaction of unsubstituted 2-mercaptoimidazole afforded product **3w** in 73% yield, while the reaction of 4,5-diphenylmercaptoimidazole afforded product **3x** in 38% yield.

Table 3. The reactions of unsymmetrical 2-mercaptobenzimidazoles with acid **1a**.



To further expand the synthetic utility of this protocol, the reactions of several unsymmetrically monosubstituted 2-mercaptobenzimidazoles were tested under the standard conditions (Table 3). The reaction of 4-methyl-2-mercaptobenzimidazole afforded **3aa** and **3ab** in 80% combined yield with good regioselectivity (**3aa**:**3ab** = 6.3:1). However, the reaction of 5-substituted 2-mercaptobenzimidazoles afforded the desired products in high yields but with poor regioselectivity. The two isomers of the reaction of each 5-substituted substrate were obtained almost in the same ratio. It is also noteworthy that isomers **3ba** and **3bb** can be separated by column chromatography while other isomers are inseparable.

We also carried out the reaction of 2-hydroxybenzimidazole **4** with **1a** under the standard conditions (Scheme 2a). Fortunately, this protocol was equally applicable to substrate **4**, although product **5** was obtained in 54% yield. Since *p*-nitrophenyl alkynyl esters have been successfully used as alkynyl acylazolium precursors in our previous work, [3b] we then tested the reaction of 4-nitrophenyl 3-phenylpropiolate **6** with **2a** using **F** as the catalyst (Scheme 2b). It was found that higher reaction temperature was essential for the complete conversion of substrate **6**, however, desired product **3a** was isolated in only 36% yield. [10] Furthermore, a scale-up synthesis of product **3a** and a derivatization of **3a** were carried out. Product **3a** was obtained in a maintained yield with a 1.5 mmol scale under the standard conditions (Scheme 2c). Reduction of compound **3a** with $LiAlH_4$ gave rise to product **7** in 56% yield whose carbonyl group and C=C double bond were reduced at the same time (Scheme 2d).



Scheme 2. Further scope exploration and synthetic application.

Conclusion

In summary, we have demonstrated an NHC-catalyzed formal [3+3] annulation of 2-mercaptobenzimidazoles or 2-mercaptoimidazoles with alkynyl acylazoliums that were directly generated from alkynyl carboxylic acids for the first time through an *in situ* activation strategy. This protocol offers a simple and rapid access to a broad range of functionalized imidazo[2,1-*b*][1,3]thiazin-4-ones, a class of skeletally interesting heterocyclic compounds. Furthermore, this protocol has the advantages of

scalability and simple manipulation in open air without inert air protection. Further investigation and application of alkynyl acylazoliums in the synthesis of diverse heterocyclic motifs are currently underway in our laboratory.

Experimental Section

General Methods and Materials.

All reactions were carried out in dry glassware, and were monitored by analytical thin-layer chromatography (TLC), which was visualized by ultraviolet light (254 nm). All solvents were obtained from commercial sources and were purified according to standard procedures. Alkynyl carboxylic acids **1**[11] and substrates **2**[12] are commercially available or prepared according to known procedures. Purification of the products was accomplished by flash chromatography using silica gel (200-300 mesh). All NMR spectra were recorded on Bruker spectrometers, running at 300 MHz or 500 MHz for ^{1}H and 75 MHz or 125 MHz for ^{13}C respectively. Chemical shifts (δ) and coupling constants (J) are reported in ppm and Hz respectively. The solvent signals were used as references (residual $CHCl_3$ in $CDCl_3$: δ_H = 7.26 ppm, δ_c = 77.0 ppm; residual residue DMSO in DMSO-d_6: δ_H = 3.3 ppm, δ_c = 39.5 ppm). The following abbreviations are used to indicate the multiplicity in NMR spectra: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet). High resolution mass spectrometry (HRMS) was recorded on TOF perimer for ESI$^+$.

General experimental procedure for the synthesis of 3

To an oven-dried 10 mL flask was charged with an acid **1** (0.18 mmol), substrate **2** (0.15 mmol), pyBOP (117 mg, 0.225 mmol), catalyst **F** (4.95 mg, 0.015 mmol), 150 mg of 4 Å MS and DIPEA (79 μL, 0.45 mmol). Then anhydrous CH_3CN (3 mL) was added to the flask and the resulting mixture was stirred in open air for typically 3-4 h until the completion of the reaction as monitored by TLC. The mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone (50:1) as the eluent to afford products **3**.

2-Phenyl-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3a). 38 mg, 92%. Yellowish solid, mp: 177-179ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.65-8.52 (m, 1H), 7.79 (d, J = 7.3 Hz, 1H), 7.70-7.67 (m, 2H), 7.61-7.40 (m, 5H), 6.91 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9, 150.6, 146.7, 142.6, 134.6, 131.7, 131.0, 129.6, 126.9, 125.9, 124.3, 118.7, 116.1, 113.8. HRMS (ESI) calcd for $C_{16}H_{11}N_2OS$ (M+H)$^+$: 279.0592, found 279.0590.

2-(*p*-Tolyl)-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3b). 42 mg, 96%. Yellowish solid, mp: 203-205ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (d, J = 7.5 Hz, 1H), 7.78 (d, J = 7.5 Hz, 1H), 7.58 (d, J = 8.2 Hz, 2H), 7.52-7.39 (m, 2H), 7.32 (d, J = 8.0 Hz, 2H), 6.88 (s, 1H), 2.42 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.0, 150.6, 146.8, 142.60, 142.55, 131.6, 131.0, 130.2, 126.7, 125.8, 124.2, 118.6, 116.1, 113.0, 21.4. HRMS (ESI) calcd for $C_{17}H_{13}N_2OS$ (M+H)$^+$: 293.0749, found 293.0740.

2-(*p*-Methoxyphenyl)-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3c). 21 mg, 45%. Yellowish solid, mp: 223-225ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (d, J = 7.4 Hz, 1H), 7.79 (d, J = 7.4 Hz, 1H), 7.66 (d, J = 6.9 Hz, 2H), 7.55-7.38 (m, 2H), 7.04 (d, J = 8.8 Hz, 2H), 6.86 (s, 1H), 3.89 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.6, 160.2, 150.2, 142.6, 132.5, 131.0, 128.4, 126.7, 125.8, 124.2, 118.6, 116.1, 114.9, 112.1, 55.6. HRMS (ESI) calcd for $C_{17}H_{13}N_2O_2S$ (M+H)$^+$: 309.0698, found 309.0697.

2-(*p*-Fluorophenyl)-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3d). 36 mg, 82%. Yellowish solid, mp: 246-248ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (d, J = 7.2 Hz, 1H), 7.80 (d, J = 6.9 Hz, 1H), 7.74-7.66 (m, 2H), 7.56-7.40 (m, 2H), 7.29-7.20 (m, 2H), 6.87 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9 (d, J = 252.7 Hz), 159.8, 149.4, 146.4, 142.7, 131.1, 130.9, 129.1 (d, J = 8.8 Hz), 126.0, 124.5, 118.8, 116.9 (d, J = 22.1 Hz), 116.2, 114.0. HRMS (ESI) calcd for $C_{16}H_{10}FN_2OS$ (M+H)$^+$: 297.0498, found 297.0491.

2-(*p*-Chloro)-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3e). 35 mg, 74%. Yellowish solid, mp: 256-258ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (d, J = 7.2 Hz, 1H), 7.81 (d, J = 7.9 Hz, 1H), 7.65 (d, J = 8.6 Hz, 2H), 7.57-7.43 (m, 4H), 6.90 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 149.3, 146.3, 142.7, 138.3, 133.1, 131.1, 129.9, 128.2, 126.1, 124.5, 118.8, 116.2, 114.1. HRMS (ESI) calcd for $C_{16}H_{10}ClN_2OS$ (M+H)$^+$: 313.0202, found 313.0195.

2-(*p*-Bromo)-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3f). 40 mg, 75%. Yellowish solid, mp: 250-252ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (d, J = 7.9 Hz, 1H), 7.81 (d, J = 7.7 Hz, 1H), 7.69 (d, J = 8.4 Hz, 2H), 7.57 (d, J = 8.4 Hz, 2H), 7.52-7.43 (m, 2H), 6.90 (s, 1H). ^{13}C NMR (75 MHz $CDCl_3$) δ 159.7, 149.4, 146.2, 142.7, 133.6, 132.9, 131.1, 128.3, 126.6, 126.1, 124.5, 118.8, 116.2, 114.2. HRMS (ESI) calcd for $C_{16}H_{10}BrN_2OS$ (M+H)$^+$: 356.9697, found 356.9689.

2-(3-Chlorophenyl)-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3g). 41 mg, 88%. Yellowish solid, mp: 192-194ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (d, J = 7.6 Hz, 1H), 7.79 (d, J = 7.4 Hz, 1H), 7.66 (s, 1H), 7.61-7.39 (m, 5H), 6.88 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.6, 148.9, 146.1, 142.5, 136.2, 135.7, 131.7, 130.9, 130.8, 127.0, 126.1, 125.1, 124.5, 118.7, 116.1, 114.5. HRMS (ESI) calcd for $C_{16}H_{10}ClN_2OS$ (M+H)$^+$: 313.0202, found 313.0190.

2-(*m*-Tolyl)-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3h). 37 mg, 85%. Yellowish solid, mp: 178-180ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (d, J = 7.6 Hz, 1H), 7.79 (d, J = 7.6 Hz, 1H), 7.56-7.30 (m, 6H), 6.89 (s, 1H), 2.45 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9, 150.8, 146.8, 142.6, 139.6, 134.5, 132.5, 131.0, 129.4, 127.4, 125.9, 124.2, 124.0, 118.6, 116.1, 113.6, 21.4. HRMS (ESI) calcd for $C_{17}H_{13}N_2OS$ (M+H)$^+$: 293.0749, found 293.0735.

2-(*o*-Fluorophenyl)-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3i). 30 mg, 68%. Yellowish solid mp: 144-146ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (d, J = 7.4 Hz, 1H), 7.80 (d, J = 7.3 Hz, 1H), 7.63 -7.40 (m, 4H), 7.36-7.22 (m, 2H), 6.92 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.6, 159.2 (d, J = 252.3 Hz), 146.7, 144.4, 142.4, 133.0 (d, J = 8.5 Hz), 130.9, 129.7, 126.0, 125.1 (d, J = 3.7 Hz), 124.3, 122.4 (d, J = 12.7 Hz), 118.6, 117.5 (d, J = 5.0 Hz), 117.0 (d, J = 21.7 Hz), 116.1. HRMS (ESI) calcd for $C_{16}H_{10}FN_2OS$ (M+H)$^+$: 297.0498, found 296.0491.

2-(2-Chlorophenyl)-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3j). 35 mg, 75%. Yellowish solid, mp: 135-137ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (d, J = 7.1 Hz, 1H), 7.81 (d, J = 6.8 Hz, 1H), 7.61-7.36 (m, 6H), 6.75 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 147.9, 146.8, 142.4, 133.3, 132.5, 131.9, 130.9, 130.7, 130.4, 127.4, 126.0, 124.3, 118.7, 118.2, 116.2. HRMS (ESI) calcd for $C_{16}H_{10}ClN_2OS$ (M+H)$^+$: 313.0202, found 313.0197.

2-(2-Bromophenyl)-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3k). 39 mg, 73%. Yellowish solid, mp: 137-139ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (d, J = 7.4 Hz, 1H), 7.80 (d, J = 7.3 Hz, 1H), 7.73 (d, J = 6.6 Hz, 1H), 7.54-7.36 (m, 5H), 6.71 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 149.6, 146.7, 142.4, 135.3, 133.9, 131.9, 130.9, 130.4, 127.9, 126.0, 124.4, 121.9, 118.7, 118.2, 116.2. HRMS (ESI) calcd for $C_{16}H_{10}BrN_2OS$ (M+H)$^+$: 356.9697, found 356.9691.

2-(Naphthalen-2-yl)-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3n). 36 mg, 73%. Yellowish solid, mp: 207-209ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (d, J = 6.7 Hz, 1H), 8.20 (s, 1H), 8.00-7.87 (m, 3H), 7.83 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 8.7 Hz, 1H), 7.66-7.41 (m, 4H), 7.04 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9, 150.5, 146.7, 142.7, 134.6, 133.0, 131.8, 131.1, 129.6, 128.9, 128.2, 127.8, 127.5, 127.3, 125.9, 124.3, 123.2, 118.7, 116.2, 114.0. HRMS (ESI) calcd for $C_{20}H_{13}N_2OS$ (M+H)$^+$: 329.0749, found 329.0742.

2-(Thiophen-2-yl)-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3o). 32 mg, 75%. Yellowish solid,

mp: 251-253°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (d, *J* = 7.4 Hz, 1H), 7.78 (d, *J* = 7.3 Hz, 1H), 7.59 (d, *J* = 4.4 Hz, 2H), 7.53-7.39 (m, 2H), 7.19 (t, *J* = 4.4 Hz, 1H), 6.91 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 145.9, 143.0, 142.7, 137.0, 130.4, 128.9, 128.7, 125.9, 124.4, 118.7, 116.1, 111.7. HRMS (ESI) calcd for $C_{14}H_9N_2OS_2$ $(M+H)^+$: 285.0156, found 285.0155.

2-Methyl-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3p). 22 mg, 69%. Yellowish solid, mp: 162-164°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (d, *J* = 7.5 Hz, 1H), 7.75 (d, *J* = 7.4 Hz, 1H), 7.49-7.38 (m, 2H), 6.52 (d, *J* = 1.1 Hz, 1H), 2.47 (d, *J* = 1.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.6, 148.7, 146.7, 142.3, 131.0, 125.8, 124.1, 118.6, 116.0, 115.5, 22.7. HRMS (ESI) calcd for $C_{11}H_9N_2OS$ $(M+H)^+$: 217.0436, found 217.0433.

2-Ethyl-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3q). 19 mg, 55%. Yellowish solid, mp: 118-120°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (d, *J* = 7.9 Hz, 1H), 7.76 (d, *J* = 7.3 Hz, 1H), 7.54-7.35 (m, 2H), 6.57 (s, 1H), 2.75 (q, *J* = 7.3 Hz, 2H), 1.39 (t, *J* = 6.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9, 155.2, 146.8, 142.4, 131.0, 125.8, 124.1, 118.5, 116.0, 113.9, 30.0, 13.5. HRMS (ESI) calcd for $C_{12}H_{11}N_2OS$ $(M+H)^+$: 231.0592, found 231.0582.

2-Pentyl-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3r). 26 mg, 64%. Yellowish solid, mp: 77-79°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.76 (dd, *J* = 7.2, 1.0 Hz, 1H), 7.49-7.38 (m, 2H), 6.54 (s, 1H), 2.70 (t, *J* = 7.9 Hz, 2H), 1.81-1.71 (m, 2H), 1.44-1.35 (m, 4H), 0.92 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 154.0, 146.8, 142.4, 131.0, 125.8, 124.1, 118.5, 116.1, 114.6, 36.7, 30.8, 28.8, 22.2, 13.8. HRMS (ESI) calcd for $C_{15}H_{17}N_2OS$ $(M+H)^+$: 273.1062, found 273.1054.

2-Cyclopropyl-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3s). 23 mg, 64%. Yellowish solid, mp: 112-114°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 (d, *J* = 7.6 Hz, 1H), 7.74 (d, *J* = 7.4 Hz, 1H), 7.54 -7.33 (m, 2H), 6.44 (s, 1H), 2.08-1.89 (m, 1H), 1.24-1.19 (m, 2H), 1.10-1.02 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.6, 156.4, 146.4, 142.5, 131.1, 125.7, 124.1, 118.5, 116.0, 111.7, 17.4, 10.3. HRMS (ESI) calcd for $C_{13}H_{11}N_2OS$ $(M+H)^+$: 243.0592, found 243.0588.

7,8-Dimethyl-2-phenyl-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3u). 41 mg, 90%. Yellowish solid, mp: 235-237°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.74-7.66 (m, 2H), 7.60-7.51 (m, 4H), 6.91 (s, 1H), 2.45, 2.43 (s×2, $2CH_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9, 150.4, 141.3, 135.1, 134.8, 133.6, 131.6, 130.3, 129.5, 129.3, 126.9, 118.8, 116.2, 113.8, 20.42, 20.37. HRMS (ESI) calcd for $C_{18}H_{15}N_2OS$ $(M+H)^+$: 307.0905, found 307.0898.

7-Phenyl-5*H*-imidazo[2,1-*b*][1,3]thiazin-5-one (3w). 25 mg, 73%. Yellowish solid, mp: 143-145°C. ^{1}H NMR (300 MHz, DMSO) δ 8.00 (d, *J* = 1.6 Hz, 1H), 7.70-7.63 (m, 2H), 7.59-7.48 (m, 3H), 7.43 (d, *J* = 1.6 Hz, 1H), 6.89 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.2, 152.5, 140.3, 134.9, 131.8, 131.7, 129.6, 127.0, 114.8, 112.1. HRMS (ESI) calcd for $C_{12}H_9N_2OS$ $(M+H)^+$: 229.0436, found 229.0426.

2,3,7-Triphenyl-5*H*-imidazo[2,1-*b*][1,3]thiazin-5-one (3x). 22 mg, 38%. Yellowish solid, mp: 230-232°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72-7.62 (m, 2H), 7.60-7.52 (m, 3H), 7.51-7.47 (m, 2H), 7.47-7.39 (m, 5H), 7.26-7.21 (m, 3H), 6.73 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 150.6, 141.0, 140.8, 134.7, 132.5, 131.6, 130.9, 129.5, 128.6, 128.2, 128.1, 127.8, 127.7, 126.80, 126.76, 113.2. HRMS (ESI) calcd for $C_{24}H_{17}N_2OS$ $(M+H)^+$: 381.1062, found 381.1057.

9-Methyl-2-phenyl-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one and 8-chloro-2-phenyl-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3aa). 35 mg, 80% combined yield. Yellowish solid, mp: 213-215°C.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.46-8.38 (m, 1H), 7.73-7.66 (m, 2H), 7.61-7.51 (m, 3H), 7.39-7.28 (m, 2H), 6.91 (s, 1H), 2.70 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 150.6, 145.8, 141.8, 134.6, 131.7, 130.7, 129.6, 128.6, 126.9, 126.4, 124.3, 113.8, 113.6, 16.6. HRMS (ESI) calcd for $C_{17}H_{13}N_2OS$ $(M+H)^+$: 293.0749, found 293.0743.

8-Methoxy-2-phenyl-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3ba). 23 mg, 50% yield. Yellowish solid, mp: 161-163°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (d, *J* = 8.9 Hz, 1H), 7.73-7.66 (m, 2H), 7.60-7.51 (m, 3H), 7.25 (d, *J* = 2.4 Hz, 1H), 7.05 (dd, *J* = 8.9, 2.4 Hz, 1H), 6.91 (s, 1H), 3.90 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 158.5, 150.3, 147.0, 143.8, 134.6, 131.7, 129.6, 126.9, 125.3, 116.6, 113.7, 113.5, 101.2, 55.7. HRMS (ESI) calcd for $C_{17}H_{13}N_2O_2S$ $(M+H)^+$: 309.0698, found 309.0695.

7-Methoxy-2-phenyl-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3bb). 22 mg, 48% yield. Yellowish solid, mp: 174-176°C.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, *J* = 2.5 Hz, 1H), 7.72-7.68 (m, 2H), 7.67 (d, *J* = 8.9 Hz, 1H), 7.58-7.52 (m, 3H), 7.12 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.89 (s, 1H), 3.94 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.3, 157.3, 150.9, 144.7, 136.9, 134.6, 131.8, 131.7, 129.9, 126.9, 119.1, 115.5, 113.5, 99.5, 56.0. HRMS (ESI) calcd for $C_{17}H_{13}N_2O_2S$ $(M+H)^+$: 309.0698, found 309.0697.

8-Methyl-2-phenyl-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3ca) and 7-methyl-2-phenyl-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3cb) (1:1 mixture). 40 mg, 91% combined yield. Yellowish solid, mp: 208-210°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (d, *J* = 8.3 Hz, 1H, 3ca), 8.39 (s, 1H, 3cb), 7.71-7.64 (m, 5H, 3ca+3cb), 7.58-7.50 (m, 7H, 3ca+3cb), 7.30 (d, *J* = 8.2 Hz, 1H, 3cb), 7.25 (d, *J* = 9.0 Hz, 1H, 3ca), 6.89 (s, 2H, 3ca+3cb) 2.55 (s, 3H, 3cb), 2.52 (s, 3H, 3ca). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 159.8, 150.6, 150.4, 145.9, 143.4, 140.7, 136.1, 134.60, 134.58, 131.7, 131.1, 129.5, 127.4, 126.9, 125.7, 118.5, 118.1, 116.1, 115.6, 113.75, 113.71, 21.82, 21.75. HRMS (ESI) calcd for $C_{17}H_{13}N_2OS$ $(M+H)^+$: 293.0749, found 293.0740.

8-Chloro-2-phenyl-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3da) and 7-chloro-2-phenyl-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-4-one (3db) (1:1 mixture). 42 mg, 90% combined yield. Yellowish solid, mp: 228-232°C.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (d, *J* = 2.0 Hz, 1H, 3db), 8.51 (d, *J* = 8.7 Hz, 1H, 3da), 7.77 (d, *J* = 1.9 Hz, 1H, 3da), 7.73-7.67 (m, 5H, 3da+3db), 7.61-7.52 (m, 6H, 3da+3db), 7.47 (dd, *J* = 8.6, 2.1 Hz, 1H, 3da or 3db), 7.42 (dd, *J* = 8.7, 2.0 Hz, 1H, 3da or 3db), 6.931 (s, 1H, 3da or 3db), 6.929 (s, 1H, 3da or 3db). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.67, 159.62, 151.1, 151.0, 147.4, 143.4, 141.2, 134.4, 132.0, 131.7, 131.4, 130.1, 129.7, 126.9, 126.6, 124.7, 119.4, 118.6, 116.8, 116.3, 113.7, 113.6. HRMS (ESI) calcd for $C_{16}H_{10}ClN_2OS$ $(M+H)^+$: 313.0202, found 313.0197.

2-Phenyl-4*H*-benzo[4,5]imidazo[2,1-*b*][1,3]oxazin-4-one (5). 21 mg, 54%. Yellowish solid, mp: 186-188°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (d, *J* = 7.3 Hz, 1H), 7.98-7.95 (m 2H), 7.76 (d, *J* = 7.7 Hz, 1H), 7.66-7.53 (m, 3H), 7.49 (td, *J* = 7.7, 1.3 Hz, 1H), 7.42 (td, *J* = 7.7, 1.2 Hz, 1H), 6.58 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 157.2, 151.4, 139.2, 132.8, 129.3, 129.1, 128.1, 126.5, 126.0, 123.9, 119.1, 115.0, 97.2. HRMS (ESI) calcd for $C_{16}H_{11}N_2O_2$ $(M+H)^+$: 263.0821, found 263.0824.

Procedure for the reduction of 3a with $LiAlH_4$

To a 25 mL round-bottom flask was charged with **3a** (41.7 mg, 0.15 mmol), 46 mg of $LiAlH_4$ (1.2 mmol) and anhydrous 4 mL of THF. The mixture was stirred at room temperature for 1h. The mixture was concentrated and the residue was purified by chromatography on silica gel using hexane/EtOAc (6:1) as the eluent to afford 22 mg of compound **5**.

2-Phenyl-3,4-dihydro-2*H*-benzo[4,5]imidazo[2,1-*b*][1,3]thiazine (5). 22 mg, 56%. Yellowish solid, mp: 164-166°C. ^{1}H NMR (300 MHz, DMSO) δ 7.64-7.36 (m, 4H), 7.31 (t, *J* = 7.4 Hz, 2H), 7.25-7.20 (m, 1H), 7.17-7.07 (m, 2H), 5.12 (t, *J* = 7.7 Hz, 1H), 3.49-3.31 (m, 2H), 2.35-2.07 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.9, 143.7, 141.6, 135.3, 128.5, 127.6, 127.4, 121.8, 121.3, 117.6, 110.5, 58.2, 47.4, 39.1. HRMS (ESI) calcd for $C_{16}H_{15}N_2S$ $(M+H)^+$: 267.0956, found 267.0960..

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References

[1] For selected reviews, see: a) A. T. Biju, N. Kuhl, F. Glorius, *Acc. Chem. Res.* **2011**, *44*, 1182; b) C.-H. Zhang, J. F. Hooper, D. W. Lupton, *ACS Catal.* **2017**, *7*, 2583; c) D. M. Flanigan, F. Romanov-Michailidis, N. A. White, T. Rovis, *Chem. Rev.* **2015**, *115*, 9307; d) W. Tang, D. Du, *Chem. Rec.* **2016**, *16*, 1489; e) X.-Y. Chen, S. Li, F. Vetica, M. Kumar, D. Enders, *iScience* **2018**, *2*, 1; f) P. Chauhan, D. Enders, *Angew. Chem. Int. Ed.* **2014**, *53*, 1485; g) A. Grossmann, D. Enders, *Angew. Chem. Int. Ed.* **2012**, *51*, 314; h) J. Izquierdo, G. E. Hutson, D. T. Cohen, K. A. Scheidt, *Angew. Chem. Int. Ed.* **2012**, *51*, 11686; i) R. S. Menon, A. T. Biju, V. Nair, *Chem. Soc. Rev.* **2015**, *44*, 5040; j) K. J. R. Murauski, A. A. Jaworski, K. A. Scheidt, *Chem. Soc. Rev.* **2018**, *47*, 1773.

[2] C. Zheng, X. Liu, C. Ma, *J. Org. Chem.* **2017**, *82*, 6940.

[3] a) C. Mou, J. Wu, Z. Huang, J. Sun, Z. Jin, Y. R. Chi, *Chem. Commun.* **2017**, *53*, 13359; b) J. Cao, K. Sun, S. Dong, T. Lu, Y. Dong, D. Du, *Org. Lett.* **2017**, *19*, 6724; c) Y. Xie, J. Wang, *Chem. Commun.* **2018**, *54*, 4597; d) C. Zhao, D. Guo, K. Munkerup, K.-W. Huang, F. Li, J. Wang, *Nat. Commun.* **2018**, *9*, 611.

[4] For selected examples, see: a) S. Mondal, S. Mukherjee, T. K. Das, R. Gonnade, A. T. Biju, *ACS Catal.* **2017**, *7*, 3995; b) Z. Jin, K. Jiang, Z. Fu, J. Torres, P. Zheng, S. Yang, B.-A. Song, Y. R. Chi, *Chem.-Eur. J.* **2015**, *21*, 9360; c) Y. Xie, C. Yu, T. Li, S. Tu, C. Yao, *Chem.-Eur. J.* **2015**, *21*, 5355; d) Y. Wang, J. Pan, J. Dong, C. Yu, T. Li, X.-S. Wang, S. Shen, C. Yao, *J. Org. Chem.* **2017**, *82*, 1790; e) J.-T. Cheng, X.-Y. Chen, S. Ye, *Org. Biomol. Chem.* **2015**, *13*, 1313; f) Y. Que, Y. Xie, T. Li, C. Yu, S. Tu, C. Yao, *Org. Lett.* **2015**, *17*, 6234; g) A. Lee, A. Younai, C. K. Price, J. Izquierdo, R. K. Mishra, K. A. Scheidt, *J. Am. Chem. Soc.* **2014**, *136*, 10589.

[5] For selected examples, see: a) X.-Y. Chen, Z.-H. Gao, C.-Y. Song, C.-L. Zhang, Z.-X. Wang, S. Ye, *Angew. Chem. Int. Ed.* **2014**, *53*, 11611; b) Y. Que, Y. Lu, W. Wang, Y. Wang, H. Wang, C. Yu, T. Li, X.-S. Wang, S. Shen, C. Yao, *Chem.-Asian J.* **2016**, *11*, 678; c) L. Zhu, C. Yu, T. Li, Y. Wang, Y. Lu, W. Wang, C. Yao, *Org. Biomol. Chem.* **2015**, *14*, 1485; d) W.-Q. Jia, H. Zhang, C.-L. Zhang, Z.-h. Gao, S. Ye, *Org. Chem. Front.* **2016**, *3*, 77; e) W. Zhang, J. Xu, J. Cao, C. Fang, J. Zhu, T. Lu, D. Du, *Tetrahedron* **2017**, *73*, 3249.

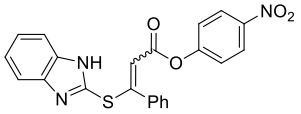
[6] For selected reviews, see: a) P. Chauhan, S. Mahajan, D. Enders, *Chem. Rev.* **2014**, *114*, 8807; b) T. Kondo, T.-a. Mitsudo, *Chem. Rev.* **2000**, *100*, 3205; c) W. Liu, X. Zhao, *Synthesis* **2013**, *45*, 2051; d) K. L. Dunbar, D. H. Scharf, A. Litomska, C. Hertweck, *Chem. Rev.* **2017**, *117*, 5521; e) D. Q. Dong, S. H. Hao, D. S. Yang, L. X. Li, Z. L. Wang, *Eur. J. Org. Chem.* **2017**, *2017*, 6576.

[7] a) C. Fang, T. Lu, J. Zhu, K. Sun, D. Du, *Org. Lett.* **2017**, *19*, 3470; b) H. Lu, J.-L. Zhang, J.-Y. Liu, H.-Y. Li, P.-F. Xu, *ACS Catal.* **2017**, *7*, 7797; c) L. He, H. Guo, Y.-Z. Li, G.-F. Du, B. Dai, *Chem. Commun.* **2014**, *50*, 3719; d) J. Chen, S. Meng, L. Wang, H. Tang, Y. Huang, *Chem. Sci.* **2015**; e) J. Chen, P. Yuan, L. Wang, Y. Huang, *J. Am. Chem. Soc.* **2017**, *139*, 7045; f) L. Yi, K.-Q. Chen, Z.-Q. Liang, D.-Q. Sun, S. Ye, *Adv. Synth. Catal.* **2017**, *359*, 44; g) Y.-T. Dong, Q. Jin, L. Zhou, J. Chen, *Org. Lett.* **2016**, *18*, 5708.

[8] For selected examples, see: a) É. V. Nosova, G. N. Liponova, M. A. Kravchenko, A. A. Laeva, V. N. Charushin, *Pharm. Chem. J.* **2008**, *42*, 169; b) X. Deng, X. Qiu, Z. Jiang, P. Zou, H. Gu, X. Li, in *Faming Zhuanli Shenqing*, CN 105085550A **2015**; c) I. Mickleburgh, F. Geng, L. Tiley, *Antiviral Chem. Chemother.* **2009**, *19*, 213; d) R. A. Glennon, S. M. Tejani-Butt, W. Padgett, J. W. Daly, *J. Med. Chem.* **1984**, *27*, 1364; e) R. A. Coburn, M. D. Taylor, W. L. Wright, *J. Pharm. Sci.* **1981**, *70*, 1322.

[9] a) J. Liu, Z. Xue, Z. Zeng, Y. x. Chen, G. Chen, *Adv. Synth. Catal.* **2016**, *358*, 3694; b) L. Veltri, G. Grasso, R. Rizzi, R. Mancuso, B. Gabriele, *Asian J. Org. Chem.* **2016**, *5*, 560; c) Z. Wang, B. Yu, X. Zhang, X. Sun, W. Bao, *Chin. J. Chem* . **2011**, *29*, 2775; d) L. Huang, J. Yang, L. Xu, X. Wu, L. Yu, W. Bao, D. Chen, *Heteroat. Chem* **2015**, *26*, 361; e) A. D. Settimo, A. M. Marini, G. Primofiore, F. D. Settimo, D. Bertini, *J. Heterocycl. Chem.* **1998**, *35*, 57; f) L. Veltri, V. Paladino, P. Plastina, B. Gabriele, *J. Org. Chem.* **2016**, *81*, 6106; g) K. M. El-Shaieb, *Phosphorus, Sulfur Silicon Relat. Elem.* **2006**, *181*, 675.

[10] In this reaction, conjugate addition byproduct shown below was isolated in 49 % yield. It was hard to convert this byproduct to **3a** even with prolonged reaction time under 80 °C.



It was also found that a large quantity of the above byproduct could be obtained and no desired product **3a** was observed when the reaction was carried out in the absence of catalyst **F** under 60 °C.

[11] a) J. Lim, J. Choi, H.-S. Kim, I. S. Kim, K. C. Nam, J. Kim, S. Lee, *J. Org. Chem.* **2016**, *81*, 303; b) D. R. Stuart, P. Alsabeh, M. Kuhn, K. Fagnou, *J. Am. Chem. Soc.* **2010**, *132*, 18326.

[12] X. Liu, M. Liu, W. Xu, M.-T. Zeng, H. Zhu, C.-Z. Chang, Z.-B. Dong, *Green Chemistry* **2017**, *19*, 5591.

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FULL PAPER

N-Heterocyclic Carbene-Catalyzed *in situ* Activation of Alkynyl Acids for C-S Bond Formation: Access to Imidazo[2,1-*b*][1,3]thiazinones

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