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Access to Imidazolidine Fused Sulfamidates and Sulfamides Bearing a Quaternary Center via 1,3-Dipolar Cycloaddition of Non-stabilized Azomethine Ylides

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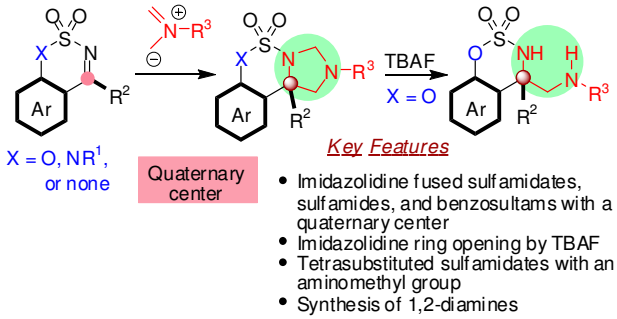
ABSTRACT



A 1,3–dipolar cycloaddition reaction of non-stabilized azomethine ylides and cyclic *N*-sulfonyl imines has been developed providing a workable access to imidazolidine fused sulfamidates, sulfamides, and benzosultams bearing a quaternary center. Distinct from the available literature, this current work enables to make entry, for the first time, into the novel imidazolidine fused sulfamidates and sulfamides. Furthermore, the selective imidazolidine ring opening accompanied by CH_2 extrusion yielded tetra-substituted sulfamidates with an aminomethyl group. In addition, imidazolidine ring opening coupled with SO_2 extrusion provided synthetically useful 1,2–diamines.

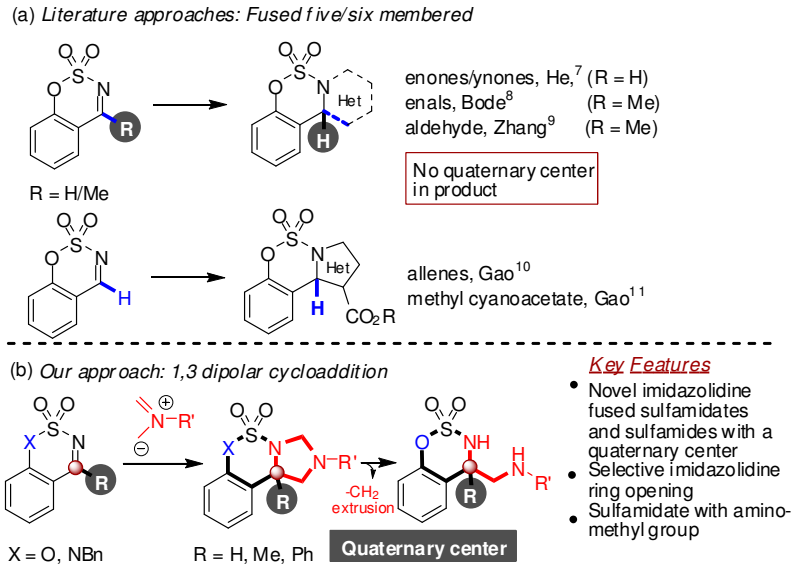
INTRODUCTION

The incorporation of a sulfonamide group is often a useful practice in medicinal chemistry for improving pharmacological potency and/or absorption, distribution, metabolism, and excretion (ADME) properties of the lead compound.[1] In an effort to mimic the pharmacological potency and ADMET properties of sulfonamides, exploration of a sulfamidate or sulfamide group has been the current trend of research in contemporary sulfonamide chemistry. This connectivity reinforces medicinal chemists to extensive designing and synthesis of sulfamidates and sulfamides. As a result, a large variety of sulfamidates including acylic and cyclic sulfamidates have been synthesized either by preparing first time,[2] or derivatization of the prepared sulfamidates.[3] However, aryl sulfamidates or their derivatives fused with nitrogen heterocycles have been limited. Perhaps most importantly, sulfamidates impart additional features when fused to a nitrogen heterocycle leading to specific biological activities.[4] While several nitrogen heterocycle fused sulfamidates have been investigated, imidazolidine fused cyclic sulfamidates remain unexplored in drug design despite imidazolidines are common integral parts of many pharmaceutical agents.[5] Imidazolidines are also attractive synthetic intermediates in organic synthesis, often employed in the preparation of 1,2-diamines.[6] In this horizon, imidazolidine fused aryl sulfamidates would be appealing although their non-availability could be a serious concern. Based upon this theme, imidazolidine fused aryl sulfamidates have appeared as an attractive synthetic target.

The synthesis of five or six membered heterocycle fused sulfamidates currently available in the literature was achieved largely by [3+2] or [4+2] annulation approaches, which are truly different from pericyclic cycloaddition reactions (Scheme 1). In 2013, He and co-workers

reported a formal [4+2]-cycloaddition of sulfamidate and enones/ynones for the synthesis of piperid-4-ones.[7] Bode et al. and Zhang et al. independently reported a protocol for the annulation of sulfamidates to the synthesis of six-membered nitrogen heterocycle fused sulfamidates using a NHC catalyst[8] or an organocatalyst.[9] A formal [3+2]-cycloaddition of *N*-arylsulfonyl imines with allenes[10] or methyl cyanoacetates[11] to the synthesis of five-membered fused sulfamidates was demonstrated by Gao et al. delivering sulfamidate fused dihydropyrroles and 2-imidazolines, respectively. While several of these fused sulfamidates have been prepared elegantly, the limitations in the current literature may include a) lacking invariably a quaternary center in the prepared fused sulfamidates, b) rare precedence of imidazolidine fused sulfamidates, and c) nitrogen heterocycle fused sulfamides hitherto been unknown.

Scheme 1. Synthetic Approaches to Nitrogen Heterocycles Fused Sulfamidates



Understanding the versatile reactivity of cyclic *N*-arylsulfonyl imine towards annulation learned from the current literature and based on our own experiences in 1,3-dipolar cycloadditions of cyclic azomethine ylides with electron-deficient alkenes,[12] we surmised that a 1,3−dipolar

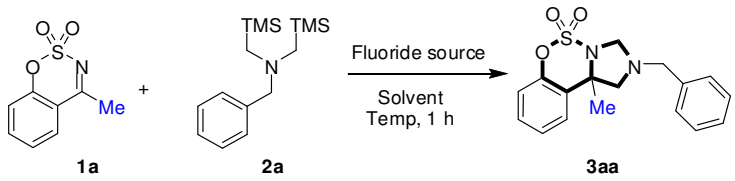
cycloaddition involving a non-stabilized azomethine ylide and cyclic *N*-arylsulfonyl imine could give a direct access to imidazolidine fused sulfamidates. However, the important questions that remain to implement this cycloaddition are, whether: a) a non-stabilized azomethine ylide could undergo 1,3–dipolar cycloaddition reaction[13] with cyclic *N*-sulfonylimines, as they could possibly undergo Michael addition,[14] b) a single, easily accessible protocol could be developed to synthesize imidazolidine fused sulfamidates bearing a quaternary center, c) a broad scope for cycloaddition reactions in terms of the preparation of sulfamidates or sulfamides, and d) use of an *N*-alkyl azomethine ylide previously unexplored. Herein, we describe 1,3-dipolar cycloaddition reactions of non-stabilized azomethine ylides and cyclic *N*-sulfonyl imines providing a workable access to novel imidazolidine fused sulfamidates, sulfamides, and benzosultams bearing a quaternary center. The key features of the current work may include synthesis of a novel class of sulfamidates and sulfamides reported for first time, previously unexplored 1,3-dipolar cycloaddition reactions of non-stabilized azomethine ylides with cyclic *N*-sulfonyl imines, nucleophile dependent ring opening of fused sulfamidates yielding tetra-substituted sulfamidates containing an aminomethyl group or 1,2-diamines.

RESULTS AND DISCUSSION

Previously, we demonstrated that cycloaddition of cyclic azomethine ylides and electron-deficient alkenes could offer an expedient access to bridged azabicyclic compounds.[12] The azomethine ylides were generated from their corresponding suitable precursors by reaction with Ag(I)F in CH_3CN at room temperature. As the reaction of azomethine ylides and *N*-sulfonyl imines have not been explored previously,[14] our initial investigation was largely focused on 1,3-dipolar cycloaddition of azomethine ylide, generated from **2a,** with a cyclic *N*-sulfonyl imine **1a**

(Table 1). Reaction of **1a** and **2a** in the presence of 2.2 equiv Ag(I)F in anhydrous DCM at room temperature gave cycloadduct **3aa** in 80% yield (entry 1). Under the condition, the azomethine ylide, generated in situ from **2a** by reaction with Ag(I)F, undergoes a [3+2]-cycloaddition with **1a** giving the cycloadduct **3a** with a quaternary center. To improve the homogeneity of the reaction, two other solvents were investigated (entries 2-3), which resulted THF as our choice. In line with our previous study,[12] other fluoride source, e.g.; CsF, or reduced molar quantity (2.0 equiv) of Ag(I)F had adverse effects (entries 4-5). Thus, an optimized condition entailed reaction of **1a** and **2a** in the presence of Ag(I)F in anhydrous THF at room temperature for 1 h affording imidazolidine fused sulfamidate **3aa** in 85% isolated yield.

Table 1. Optimization Study[a]



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

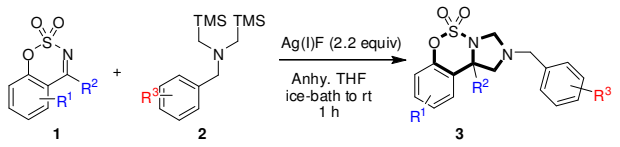
Entry	Fluoride source	Solvent	Yield of **3aa** (%)
1	AgF	Anhy. DCM	80
2	AgF	Anhy. THF	85
3	AgF	Anhy. CH_3CN	43
4	CsF	Anhy. THF	00
5[b]	AgF	Anhy. THF	71

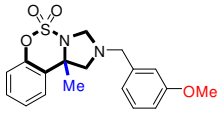
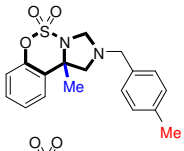
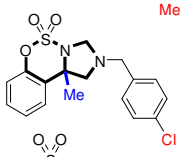
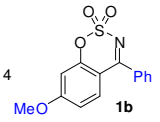
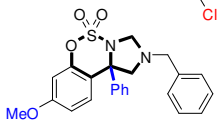
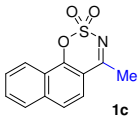
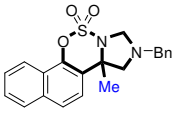
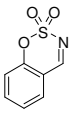
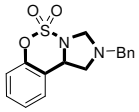
[a] **1a** (0.2 mmol), **2a** (0.22 mmol), fluoride source (0.44 mmol), temp., 1 h; [b] 2.0 equiv AgF

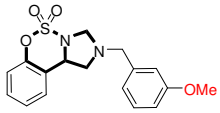
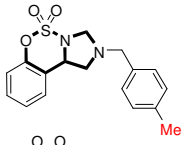
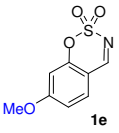
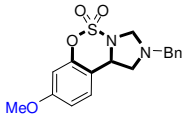
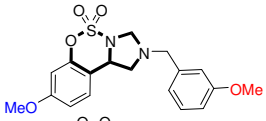
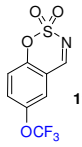
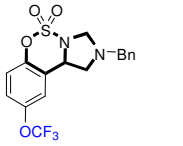
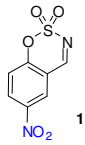
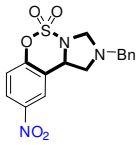
The cyclic *N*-sulfonyl aldimines or ketimines **1a-g and 4a-c** were prepared by the reaction of 2-hydroxy benzaldehydes or acetophenones or 2-amino acetophenones and sulfamoyl chloride (see the Supporting Information).[9-10] The azomethine ylide precursors **1a-f** were easily prepared from their corresponding amines that are commercially available.[12] Thus, heating benzylamine (1 equiv) and iodomethyltrimethylsilane (2.5 equiv) in the presence of powdered K_2CO_3 in anhydrous MeCN at 90 ^oC for 72 h gave the azomethine ylide precursors (see the Supporting Information). The study was subsequently extended to establish the scope of 1,3–dipolar cycloaddition of different azomethine ylides with cyclic *N*-sulfonyl imines (Scheme 2). The reaction of azomethine ylide **2b** bearing an electron-donating -OMe group at the *meta*-position of aryl ring afforded **3ab** in 90% yield (entry 1). The other azomethine ylide precursors bearing –Me or –Cl group at the *para*-position when reacted with sulfamidate **1a**, gave the desired products **3ac** and **3ad** in 89% and 83% yields, respectively (entry 2-3). Likewise, when sulfamidate **1b** having a phenyl group on imine double bond was reacted with azomethine ylide **2a**, it also produced imidazolidine fused sulfamidate **3ba** in 75% yield (entry 4). *N*-ASulfonyl imine **1b** embedded in a naphthalene ring was also a viable substrate affording **3ba** although in somewhat reduced yield (65%) (entry 5). The scope of 1,3-dipolar cycloaddition was also extended to the cyclic *N*-arylsulfonyl aldimines. While the reaction of unsubstituted aldimine **1d** and azomethine ylide **2a** gave **3da** in 88% (entry 6), reaction of **1d** and azomethine ylide, generated in situ from the precursor **2b or 2c**, afforded **3db** and **3dc** in 92% and 89% yields, respectively (entry 7-8). When the azomethine ylide, generated in situ from **2a** was subjected to the reaction with **1e**, the cycloadduct **3ea** was obtained in 75% yield (entry 9). However, an improved yield of 86% was observed when -OMe substituent was present on both the reacting partners, yielding imidazolidine fused sulfamidate **3eb** in 86% yield (entry 10). A substrate **1f**

containing an OCF_3 group also underwent cycloaddition producing imidazolidine fused sulfamidates **3fa** in excellent yield (entry 11).

Scheme 2. Synthesis of Imidazolidine Fused Sulfamidates by [3+2]-Cycloaddition



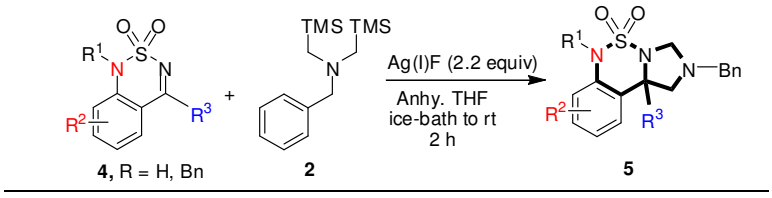
Entry	Sulfamidate	Azomethine ylide	Product	Yield
1	**1a**	**2b** R_3 = 3-OMe		**3ab** (90%)
2	**1a**	**2c** R_3 = 4-Me		**3ac** (89%)
3	**1a**	**2d** R_3 = 4-Cl		**3ad** (83%)
4	 **1b**	**2a** R_3 = H		**3ba** (75%)
5	 **1c**	**2a**		**3ca** (65%)
6	 **1d**	**2a**		**3da** (88%)

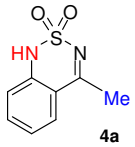
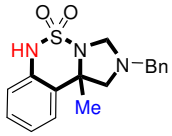
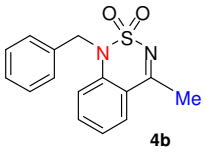
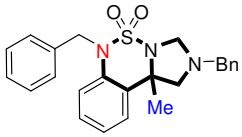
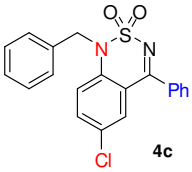
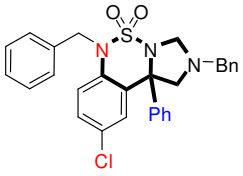
Entry	Sulfamidate	Azomethine ylide	Product	Yield
7	**1d**	**2b**		**3db** (92%)
8	**1d**	**2c**		**3dc** (89%)
9	 **1e**	**2a**		**3ea** (75%)
10	**1e**	**2b**		**3eb** (86%)
11	 **1f**	**2a**		**3fa** (80%)
12	 **1g**	**2a**		**3ga** (68%)

However, compound **1g** with an electron-withdrawing group exerts diminishing effect producing **3ga** in reduced yield (68%) (entry 12). Central to this investigation was the realization, for the first time, of a 1,3-dipolar cycloaddition of non-stabilized ylides and cyclic *N*-arylsulfonyl imines, which could smoothly occur under a mild condition affording imidazolidine fused sulfamidates containing a quaternary center.

Furthermore, the compatibility of a nitrogen analogue of *N*-arylsulfonyl imines towards cycloaddition with the non-stabilized azomethine ylides was studied (Scheme 3).

Scheme 3. Synthesis of Imidazolidine Fused Cyclic Sulfamides



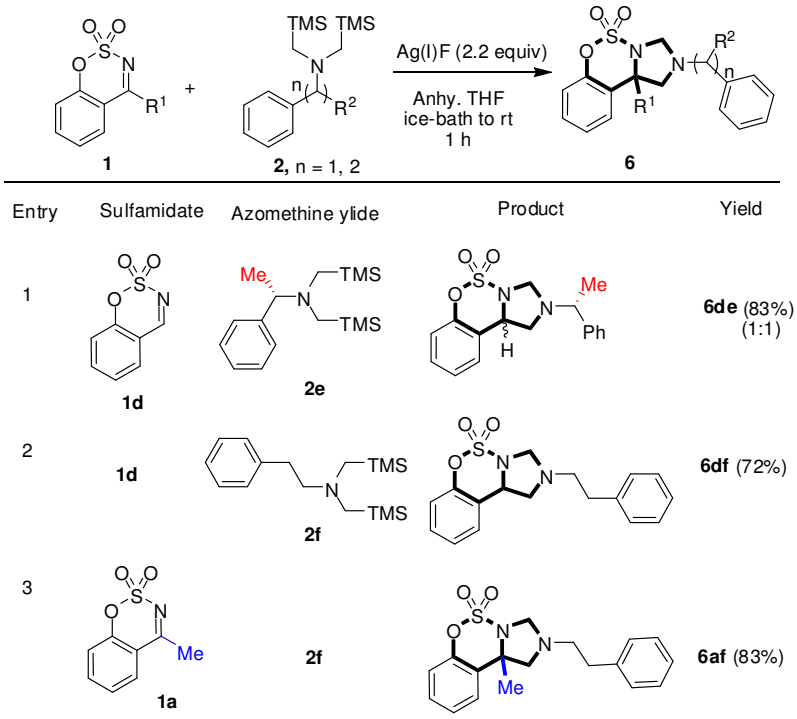
Entry	Sulfamide	Azomethine ylide	Product	Yield
1	 **4a**	**2a**		**5aa** (0%)
2	 **4b**	**2a**		**5ba** (60%)
3	 **4c**	**2a**		**5ca** (54%)

Disappointingly, the reaction of **4a** and azomethine ylide **2a** under the standard conditions did not form the cycloadduct **5aa** (entry 1). This could be attributed to the free NH group present in **4a**. Indeed, *N*-benzyl protection in **4a** largely stopped this adventitious problem. Thus, cycloaddition of azomethine ylide derived from **2a** underwent smooth [3+2]-addition with **4b** producing cycloadduct **5ba** in 60% yield (entry 2). Likewise, **2a** underwent smooth [3+2]-addition with **4c** containing a phenyl group affording cycloadduct **5ca** in 54% yield (entry 3). Pivotal to this investigation was to uncover the use of *N*-arylsulfonyl imine **4b-4c** as suitable reactant partners in the 1,3-dipolar

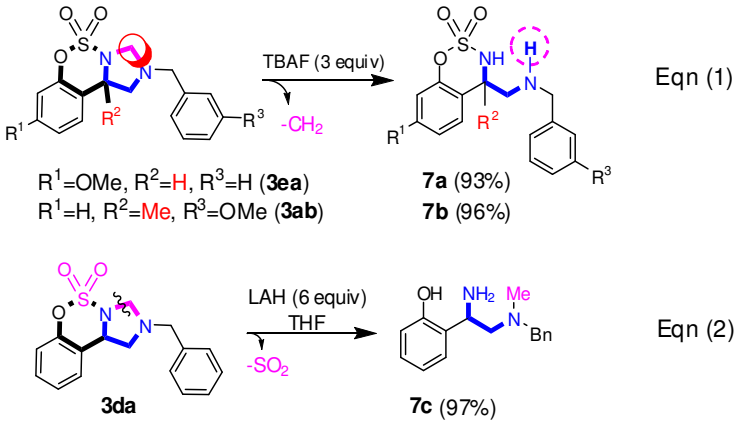
cycloaddition reaction of azomethine ylides yielding imidazolidine fused sulfamides **5ba-5ca** bearing a quaternary center that were previously unknown.

The wide scope of the cycloaddition was further demonstrated in the synthesis of enantiomerically pure imidazolidine fused sulfamidates (Scheme 4). The cycloaddition of the azomethine ylide derived from precursor **3e** containing a stereocenter at the benzylic position was investigated. Thus, when chiral azomethine ylide **3e** was employed in the cycloaddition reaction with **1d**, two diastereomers were formed in a 1:1 ratio with a combined 83% yield of **6de** (entry 1). The two diastereoisomers were easily separated by flash silica chromatography and distinguished by proton NMR spectroscopy. While the aforesaid 1,3-dipolar cycloadditions involve *N*-benzyl azomethine ylides, preparation of *N*-alkyl azomethine ylides and their cycloadditons with electron-deficient alkenes remain unexplored. Gratifyingly, azomethine ylide derived from the precursor **2f** undergoes cycloaddition eventfully with **1d** delivering imidazolidine fused sulfamidate **6df** in 72% yield (entry 2). Moreover, **2f** also reacted smoothly with **1a** giving sulfamidate **6af** with 83% yield (entry 3). The key features of this part of investigation were: a) demonstration, for the first time, of a 1,3−dipolar cycloaddition involving chiral azomethine ylides and *N*-arylsulfonyl imine, b) the use of *N*-alkyl azomethine ylides in 1,3−dipolar cycloaddition with *N*-sulfonyl imine furnishing sulfamidates containing a quaternary center.

Scheme 4. **Synthesis of other Imidazolidine Fused Cyclic Sulfamidates**

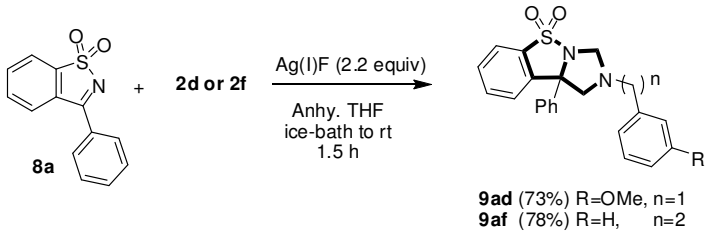


A selective ring opening of the imidazolidine ring in imidazolidine fused sulfamidates while elusive could potentially be used to prepare tetra-substituted sulfamidates. Treatment of **3ea** and **3ab** with TBAF (3 equiv) in THF at 80 °C gave tetra-substituted sulfamidates **7a-7b** in 93-96% yield (Eqn 1). The cleavage of imidazolidine ring is accompanied by -CH_2 extrusion yielding tetra-substituted sulfamidates containing an aminomethyl functionality that could be used as a synthetic handle for further chemical transformation. Distinct from the literature, the selective ring opening of imidazolidine ring could complement the reported conditions performed under strong acidic conditions.[8] In contrast, when imidazolidine fused sulfamidate **3da** was treated with LAH, we observed SO_2 extrusion as well as C-N bond cleavage of imidazolidine generating 1,2-diamine functionality in *ortho*-phenol and formed compound **7c** in 97% yield (Eqn 2). Thus, distinct from the literature reports, nucleophile dependent ring opening of imidazolidine fused sulfamidates paved ways to the synthesis of 1,2-diamine derivatives.



More recently, five membered benzosultams received special attention to synthetic chemists for variety of derivatization.[15] Thus, the protocol was further extended to benzosultam where O or N is absent (Scheme 5). Under the standard conditions, reaction of **8a** with azomethine ylide precursor **2d** or **2f** afforded imidazolidine fused benzosultams **9ad** and **9af** in excellent yields (73% and 78%, respectively) bearing a quaternary center. The synthesis of such fused heterocycle with a quaternary center is unknown in the literature.

Scheme 5. **Imidazolidine Fused Benzosultam Synthesis**



In summary, we have developed a protocol for the synthesis of novel class of compounds, imidazolidine fused sulfamidates, sulfamides and benzosultams bearing a quaternary center. The chemistry developed to prepare these compounds involve a 1,3−dipolar cycloaddition reaction of non-stabilized azomethine ylides and *N*-arylsulfonyl aldimine or ketimines. Furthermore, the selective imidazolidine ring opening accompanied by CH_2 extrusion generated tetra-substituted

sulfamidates with an aminomethyl group. In addition, imidazolidine ring opening coupled with SO_2 extrusion provided synthetically useful 1,2−diamines.

EXPERIMENTAL SECTION

General Methods. Unless noted otherwise, all reagents and solvents were purchased from commercial sources and used as received. All reactions were performed in a screw-capped vial. The proton (^{1}H) and carbon (^{13}C) NMR spectra were obtained using a 400 MHz using Me_4Si as an internal standard and are reported in δ units. Coupling constants (J values) are reported in Hz. Column chromatography was performed on silica gel (100−200#, 230-400#). High resolution mass spectra (HRMS) were obtained using the electron spray ionization (ESI) technique and as TOF mass analyzer. IR spectra are reported in cm^{-1} units. All melting points were taken using a melting point apparatus equipped with a calibrated thermometer and are uncorrected. Following compounds were prepared according to literature procedure: 4-Methylbenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (**1a**),[9a] N-Benzyl-1-(trimethylsilyl)-N-((trimethylsilyl)methyl) methanamine (**2a**),[16] 4-Methylnaphtho[2,1-*e*][1,2,3]oxathiazine 2,2-dioxide (**1c**),[9a] Benzo[*e*][1,2,3]oxathiazine 2,2-dioxide (**1d**),[10] 7-Methoxybenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (**1e**),[10] 6-Nitrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (**1g**),[17] 4-Methyl-1H-benzo[*c*][1,2,6] thiadiazine 2,2-dioxide (**4a**)[18] 3-phenylbenzo[*d*]isothiazole 1,1-dioxide (**8a**)[19]

General Procedure for the Synthesis of Azomethine ylide Precursors (**2a-f**)

In an oven-dried screw-cap vial (15 mL) with a magnetic bar, benzylamine (1 mmol), iodomethyltrimethylsilane (2.5 mmol), and powdered K_2CO_3 (5 mmol) were taken. (Note: powdered K_2CO_3 was oven-dried at 100 °C for 2 h before use). The reagents were purged twice with nitrogen. Under nitrogen atmosphere, anhydrous acetonitrile (5 mL) was added, and the septum was replaced with a teflon coated screw cap. The reaction mixture was heated at 90 °C for 72 h. Then, the reaction mixture was passed through a small celite bed, and the bed was washed with ethyl acetate (10 mL). The filtrate was concentrated under vacuum and purified by neutral alumina column chromatography with 100% hexane or 1% (ethyl acetate: hexane) as eluent.

*General Procedure for the Synthesis of Imidazolidine Fused Sulfamidates (**3**, **6**), Sulfamides (**5**) and Benzosultam **(9)***

In an oven-dried aluminium foil coated screw-cap vial with a magnetic bar, cyclic sulfonylimine (0.2 mmol, 1 equiv) and Ag(I)F (0.44 mmol, 2.2 equiv) were taken. [Note: Ag(I)F was completely dried under vacuum at 55-60 °C at least for 30 min with aluminium foil coating before use]. The vial was purged three times with nitrogen and kept under ice bath. A solution of the azomethine ylide precursor (0.22 mmol, 1.1 equiv) in anhydrous THF (1 mL) was added dropwise . The ice-bath was removed, and the reaction mixture was stirred at room temperature for 1-2 h under nitrogen atmosphere. The reaction was monitored by TLC. Then, the reaction mixture was diluted with 5 mL CH_2Cl_2 and passed through a celite bed. The filtrate was concentrated *in vacuo* and purified by column chromatography (100-200# silica, ethyl acetate : hexane) to give the desired imidazolidine fused sulfamidate or sulfamide or benzosultam.

*General Procedure for the -CH_2 Extrusion Reaction (compound **7a-b**)*

To a solution of imidazolidine fused sulfamidate (0.2 mmol) in anhydrous THF (1 mL), TBAF▪3H2O (3 equiv) was added, and the reaction mixture was heated at 80 ^{o}C for 5 h. Silica gel (100-200#) was added to the reaction mixture, and the excess solvent was evaporated. The silica gel mixed with the crude product was loaded on the column, which upon chromatography (ethyl acetate /hexane = 3:7 – 7:3) afforded the desired product.

*General Procedure for the -SO_2 Extrusion Reaction (compound **7c**)*

To a suspension of lithium aluminum hydride (27 mg, 0.72 mmol) in anhydrous THF (1 mL), [Note: *LAH should be handled very carefully due to its explosive nature*] solution of imidazolidine fused sulfamidate (40 mg. 0.12 mmol) was added drop wise under ice-cooling. The mixture was refluxed for 6 hr and cooled naturally to room temperature, and then to 0 °C with an ice bath. The reaction mixture was quenched by drop wise addition 10% NaOH solution (1 mL) at 0 °C and stirred for 30 min at same temperature. The resulting suspension was passed through celite bed and filtrate was concentrated *in vacuo*. The crude was purified by short column chromatography (100-200# silica) with ethyl acetate as an eluent to get desire product.

2-Benzyl-10*b*-methyl-1,2,3,10*b*-tetrahydrobenzo[*e*]imidazo[1,5-*c*][1,2,3]oxathiazine 5,5-dioxide (3aa): Pale yellow oil; Yield 85% (56 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.23 (m, 4H), 7.20 (dt, J = 7.5, 1.3 Hz, 1H), 7.15–7.10 (m, 3H), 7.02 (dd, J = 8.2, 1.4 Hz, 1H), 4.43 (d, J = 7.0 Hz, 1H), 4.16 (d, J = 7.0 Hz, 1H), 3.71–3.59 (m, 2H), 3.29 (d, J = 10.3 Hz, 1H), 3.06 (d, J = 10.3 Hz, 1H), 1.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.9, 137.1, 129.1, 128.6, 128.4, 127.6, 127.5, 126.6, 125.9, 119.0, 72.7, 69.1, 68.8, 57.2, 27.4; HRMS (ESI-TOF) m/z: [M

+ H]$^+$ Calcd for $C_{17}H_{19}N_2O_3S$ 331.1116; Found 331.1112; IR (Neat): 3029, 2925, 2853, 1448, 1398, 1179 cm^{-1}.

7-Methoxy-4-phenylbenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (1b)[18]: Off-white solid; 67% Yield (97 mg); mp. 139-140 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78–7.72 (m, 2H), 7.71–7.65 (m, 1H), 7.61−7.54 (m, 3H), 6.91−6.86 (m, 2H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.9, 171.4, 166.5, 157.1, 134.1, 133.4, 132.9, 130.5, 128.8, 113.1, 109.9, 103.6, 56.4, 45.0; HRMS (ESI-TOF) m/z: [M]$^+$ Calcd for $C_{14}H_{11}NO_4S$ 289.0409; Found 289.0412; IR (KBr): 3062, 2927, 2814, 1320, 1171 cm^{-1}.

6-(Trifluoromethoxy)benzo[*e*][1,2,3]oxathiazine 2,2-dioxide (1f): To a solution of 2-hydroxy-5-(trifluoromethoxy)benzaldehyde (1.0 mmol) in DMA (1 mL) at room temperature was added freshly prepared $ClSO_2NH_2$ (2.0 mmol, prepared according to reported procedure[10]) in small portions, and the resulting solution was stirred for 18 h. The reaction was quenched with ice-cold H_2O (10 mL), and CH_2Cl_2 (20 mL) was added to the water. The aqueous layer was separated and extracted with CH_2Cl_2 (2 x 10 mL), and the combined organic layers were washed with saturated $NaHCO_3$ solution (50 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The crude product was purified by small column chromatography to obtain the desired product **7** as brown yellow oil (67% yield, 178 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.71 (s, 1H), 7.67–7.61 (m, 1H), 7.60 (s, 1H), 7.40 (d, J = 9.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.5, 152.3, 146.0, 130.4, 122.6, 120.2 (q, J = 258 Hz), 120.6, 115.8; HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_8H_5F_3NO_4S$ 267.9891; Found 267.9897.

N-(3-Methoxybenzyl)-1-(trimethylsilyl)-N-((trimethylsilyl)methyl)methanamine (2b): Transparent liquid; Yield 70% (228 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 (t, J = 7.8Hz, 1H), 6.96 (d, J = 2.0Hz, 1H), 6.92 (d, J = 6.9 Hz, 1H), 6.79 (dd, J = 7.8, 2.1 Hz, 1H), 3.83 (s, 3H),

3.40 (s, 2H), 1.92 (s, 4H), 0.07−0.05 (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 142.8, 129.0, 121.0, 113.7, 112.4, 66.1, 55.1, 50.5, -1.2; HRMS (ESI-TOF) m/z: $[M]^+$ Calcd for $C_{16}H_{31}NOSi_2$ 309.1944; Found 309.1951; IR (Neat): 3029, 2954, 1602, 1448, 1247 cm^{-1}.

N-(4-Methylbenzyl)-1-(trimethylsilyl)-N-((trimethylsilyl)methyl)methanamine (2c): Transparent liquid; 73% Yield (213 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.22 (d, J = 8.0 Hz, 2H), 7.16–7.12 (d, J = 8.0 Hz, 2H), 3.40 (s, 2H), 2.37 (s, 3H), 1.92 (s, 4H), 0.07 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.7, 133.4, 131.2, 129.4, 66.5, 51.6, -0.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{32}NSi_2$ 294.2073; Found 294.2079; IR (Neat): 3032, 2956, 1611, 1245 cm^{-1}.

N-(4-Chlorobenzyl)-1-(trimethylsilyl)-N-((trimethylsilyl)methyl)methanamine (2d): Transparent liquid; 82% Yield (256 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.26 (m, 4H), 7.16–7.12 (m, J = 8.0 Hz, 2H), 3.40 (s, 2H), 2.37 (s, 3H), 1.92 (s, 4H), 0.09 - 0.05 (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.6, 133.4, 131.2, 129.4, 66.5, 51.6, -0.01; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{29}ClNSi_2$ 314.1527; Found 314.1529; IR (Neat): 3029, 2955, 1607, 1247 cm^{-1}.

(*S*)-1-Phenyl-N,N-bis((trimethylsilyl)methyl) ethanamine (2e): Transparent liquid; Yield 70% (205 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, J = 7.8 Hz, 2H), 7.34 (t, J = 7.7 Hz, 2H), 7.24 (d, J = 7.2 Hz, 1H), 3.94 (q, J = 6.6 Hz, 1H), 1.91 (dd, J = 14.5 Hz, 4H), 1.30 (d, J = 6.5 Hz, 4H), 0.05 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.0, 128.1, 127.6, 126.3, 60.7, 44.4, 9.2, -1.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{32}NSi_2$ 294.2073; Found 294.2077; IR (Neat): 3030, 2955, 2926, 1662, 1453, 1248, cm^{-1}.

2-Phenyl-N,N-bis((trimethylsilyl)methyl)ethanamine (2f): Transparent liquid; Yield 82% (243 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.27 (m, 2H), 7.22−7.20 (m, 3H), 2.74 (dd, J = 10.8, 6.8 Hz, 1H), 2.64 (dd, J = 10.8, 6.8 Hz, 1H), 2.05 (s, 4H), 0.11–0.05 (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.0, 128.9, 128.3, 125.7, 63.0, 50.2, 33.1, -1.1; HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{32}NSi_2$ 294.2073; Found 294.2075; IR (Neat): 3028, 2954, 2926, 1660, 1455, 1248 cm^{-1}.

2-(3-Methoxybenzyl)-10*b*-methyl-1,2,3,10*b*-tetrahydrobenzo[*e*]imidazo[1,5-c][1,2,3]oxathiazine 5,5-dioxide (3ab): Light yellow oil; Yield 90% (65 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32−7.26 (m, 1H), 7.23−7.11 (m, 3H), 7.02 (dd, J = 8.3, 1.3 Hz, 1H), 6.78 (dd, J = 8.2, 2.4Hz, 1H), 6.74−6.67 (m, 2H), 4.47 (d, J = 7.0 Hz, 1H), 4.15 (d, J = 7.0 Hz, 1H), 3.70 (s, 3H), 3.62 (s, 2H), 3.30 (d, J = 10.0 Hz, 1H), 3.03 (d, J = 10.3 Hz, 1H), 1.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 150.0, 138.7, 129.5, 129.1, 127.5, 126.6, 125.8, 120.6, 118.9, 113.4, 72.7, 69.2, 68.7, 56.9, 55.1, 27.3; HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{18}H_{21}N_2O_4S$ 361.1222; Found 361.1225; IR (Neat): 3038, 2923, 1447, 1387 cm^{-1}.

10*b*-Methyl-2-(4-methylbenzyl)-1,2,3,10*b*-tetrahydrobenzo[*e*]imidazo[1,5-*c*][1,2,3] oxathiazine 5,5-dioxide (3ac): Off-white solid; 89% Yield (61 mg); mp. 111-113 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35−7.29 (m, 1H), 7.23 (dt, J = 7.5, 1.3 Hz, 1H), 7.18−7.13 (m, 1H), 7.13−7.09 (m, 2H), 7.08−7.02 (m, 3H), 4.45 (d, J = 7.0 Hz, 1H), 4.18 (d, J = 7.0 Hz, 1H), 3.70−3.58 (m, 2H), 3.31 (d, J = 10.3 Hz, 1H), 3.08 (d, J = 10.3 Hz, 1H), 2.35 (s, 3H), 1.87 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.8, 137.3, 133.9, 129.2, 129.0, 128.4, 127.5, 126.5, 125.8, 118.9, 72.7, 69.0, 68.7, 56.9, 27.4, 21.1; HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{18}H_{21}N_2O_3S$ 345.1273; Found 345.1277; IR (KBr): 2980, 2829, 1580, 1449, 1397, 1175 cm^{-1}.

2-(4-Chlorobenzyl)-10*b*-methyl-1,2,3,10*b*-tetrahydrobenzo[*e*]imidazo[1,5-*c*][1,2,3] oxathiazine 5,5-dioxide (3ad): Off-white solid; 83% Yield (60 mg); mp. 118-120 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.30 (m, 1H), 7.30–7.20 (m, 3H), 7.18–7.12 (m, 1H), 7.12–7.02 (m, 3H), 4.46 (d, J = 7.0 Hz, 1H), 4.16 (d, J = 7.0 Hz, 1H), 3.70–3.57 (m, 2H), 3.30 (d, J = 10.3 Hz, 1H), 3.06 (d, J = 10.3 Hz, 1H), 1.87 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.9, 135.6, 133.4, 129.6, 129.2, 128.7, 127.4, 126.5, 125.9, 118.9, 72.6, 69.1, 68.7, 56.4, 27.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{18}ClN_2O_4S$ 365.0727; Found 365.0729; IR (KBr): 2989, 2829, 1613, 1488, 1397 cm^{-1}.

2-Benzyl-8-methoxy-10*b*-phenyl-1,2,3,10*b*-tetrahydrobenzo[*e*]imidazo[1,5-*c*][1,2,3] oxathiazine 5,5-dioxide (3ba): Transparent oil; 75% Yield (48 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59–7.53 (m, 2H), 7.41–7.29 (m, 6H), 7.28–7.23 (m, 2H), 7.07 (d, J = 8.5 Hz, 1H), 6.84 (dd, J = 8.7, 2.6 Hz, 1H), 6.69 (d, J = 2.5 Hz, 1H), 4.47 (t, J= 6.5 Hz, 2H), 3.88 (s, 3H), 3.77–3.65 (m, 3H), 3.40 (d, J = 10.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.2, 151.3, 141.5, 137.1, 129.5, 128.6, 128.5, 128.3, 128.1, 127.7, 127.7, 116.3, 112.3, 103.9, 73.4, 73.0, 70.0, 57.3, 55.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{23}N_2O_4S$ 423.1379; Found 423.1382; IR (Neat): 3062, 3027, 2927, 2814, 1452, 1320 cm^{-1}.

2-Benzyl-3*a*-methyl-1,2,3,3*a*-tetrahydroimidazo[1,5-*c*]naphtho[2,1-*e*][1,2,3]oxathiazine 11,11-dioxide (3ca): Pale yellow oil; Yield 65% (49 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27–8.21 (m, 1H), 7.88–7.83 (m, 1H), 7.71 (d, J = 8.5 Hz, 1H), 7.66–7.58 (m, 2H), 7.30–7.27 (m, 3H), 7.19–7.13 (m, 3H), 4.53 (d, J = 7.0 Hz, 1H), 4.27 (d, J = 7.0 Hz, 1H), 3.75–3.65 (m, 2H), 3.42 (d, J = 10.5 Hz, 1H), 3.17 (d, J = 10.3 Hz, 1H), 1.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.9, 137.0, 133.5, 128.5, 128.2, 127.6, 127.5, 127.4, 127.3, 125.6, 125.4, 124.6,

122.7, 121.9, 121.3, 72.8, 69.2, 68.3, 57.4, 27.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{21}N_2O_3S$ 381.1273; Found 381.1281; IR (Neat): 2959, 2855, 1634, 1459, 1276 cm^{-1}.

2-Benzyl-1,2,3,10*b*-tetrahydrobenzo[*e*]imidazo[1,5-*c*][1,2,3]oxathiazine 5,5-dioxide (3da): Transparent oil; Yield 88% (56 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.30-7.38 (m, 4H), 7.25 - 7.29 (m, 2H), 7.23 (td, *J* = 8, 1 Hz, 1H), 7.05 - 7.11 (m, 2H), 5.17 (dd, *J* = 6.5, 4.8 Hz, 1H), 4.42 (d, *J* = 7.5 Hz, 1H), 4.25 (d, *J* = 7.3 Hz, 1H), 3.83–3.68 (m, 2H), 3.53 (ddd, *J* = 11.2, 6.7, 0.8 Hz, 1H), 3.21 (dd, *J* = 11.0, 4.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.8, 137.0, 129.1, 128.6, 128.5, 128.4, 127.6, 126.5, 125.8, 118.9, 72.7, 61.6, 59.9, 57.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{17}N_2O_3S$ 317.0960; Found 317.0963; IR (Neat): 2925, 2854, 1399, 1179 cm^{-1}.

2-(3-Methoxybenzyl)-1,2,3,10*b*-tetrahydrobenzo[*e*]imidazo[1,5-*c*][1,2,3]oxathiazine 5,5-dioxide (3db): Pale yellow oil; Yield 92% (64 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.35–7.29 (m, 1H), 7.27–7.17 (m, 2H), 7.11–7.05 (m, 2H), 6.87–6.81 (m, 3H), 5.16 (dd, *J* = 6.5, 4.5 Hz, 1H), 4.43 (d, *J* = 7.3 Hz, 1H), 4.23 (d, *J* = 7.3 Hz, 1H), 3.77 (s, 3H), 3.74 (s, 2H), 3.55–3.47 (m, 1H), 3.20 (dd, *J* = 11.0, 4.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 150.5, 138.9, 129.6, 129.1, 126.5, 125.9, 122.8, 120.8, 119.1, 113.8, 113.4, 72.3, 61.5, 60.0, 57.7, 55.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{19}N_2O_4S$ 347.1066; Found 347.1061; IR (Neat): 2926, 2836, 1600, 1585, 1488, 1397 cm^{-1}.

2-(4-Methylbenzyl)-1,2,3,10*b*-tetrahydrobenzo[*e*]imidazo[1,5-*c*][1,2,3] oxathiazine 5,5-dioxide (3dc): Transparent oil; 89% Yield (58 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.37–7.30 (m, 1H), 7.26–7.20 (m, 1H), 7.16 (s, 4H), 7.08 (d, *J* = 8.3 Hz, 2H), 5.17 (dd, *J* = 6.3, 4.8 Hz, 1H), 4.41 (d, *J* = 7.3 Hz, 1H), 4.25 (d, *J* = 7.3 Hz, 1H), 3.78–3.66 (m, 2H), 3.56–3.46 (m, 1H), 3.20 (dd, *J* = 11.2, 4.6 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5, 137.4,

134.2, 129.3, 129.0, 128.6, 126.5, 125.9, 122.8, 119.1, 72.3, 61.5, 59.9, 57.6, 21.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{19}N_2O_3S$ 331.1116; Found 331.1119; IR (Neat): 2980, 2829, 1580, 1449, 1397, 1175 cm^{-1}.

2-Benzyl-8-methoxy-1,2,3,10*b*-tetrahydrobenzo[*e*]imidazo[1,5-*c*][1,2,3]oxathiazine 5,5-dioxide (3ea): Pale yellow oil; Yield 75% (52 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.28–7.22 (m, 3H), 7.20–7.16 (m, 2H), 6.86 (dd, J = 8.7, 0.6 Hz, 1H), 6.70 (dd, J = 8.7, 2.6 Hz, 1H), 6.51 (d, J = 2.5 Hz, 1H), 5.02 (dd, J = 6.3, 4.5 Hz, 1H), 4.31 (d, J = 7.3 Hz, 1H), 4.16–4.10 (m, 1H), 3.74 (s, 3H), 3.67 (d, J = 3.3 Hz, 2H), 3.39 (ddd, J = 11.0, 6.5, 0.8 Hz, 1H), 3.08 (dd, J = 11.0, 4.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 151.2, 137.3, 128.6, 127.7, 127.1, 114.4, 112.8, 103.9, 72.2, 61.6, 59.6, 58.0, 55.6; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{19}N_2O_4S$ 347.1066; Found 347.1071; IR (Neat): 3029, 2956, 2924, 1662, 1449 cm^{-1}.

8-Methoxy-2-(3-methoxybenzyl)-1,2,3,10*b*-tetrahydrobenzo[*e*]imidazo[1,5-*c*][1,2,3] oxathiazine 5,5-dioxide (3eb): Pale yellow oil; Yield 86% (64 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.23–7.28 (m, 1H), 6.93–6.98 (m, 1H), 6.82–6.87 (m, 3H), 6.78 (dd, J = 8.5, 2.5 Hz, 1H), 6.60 (d, J = 2.5 Hz, 1H), 5.11 (dd, J = 6.3, 4.3 Hz, 1H), 4.41 (d, J = 7.3 Hz, 1H), 4.22 (d, J = 7.3 Hz, 1H), 3.82 (s, 3H), 3.79 (s, 3H), 3.74 (s, 2H), 3.43–3.51 (m, 1H), 3.17 (dd, J = 11.0, 4.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 159.8, 151.2, 138.9, 129.6, 127.1, 120.8, 114.4, 113.8, 113.3, 112.8, 103.9, 72.2, 61.6, 59.6, 57.8, 55.7, 55.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{21}N_2O_5S$ 377.1171; Found 377.1166; IR (Neat): 2925, 2847, 1483, 1445 cm^{-1}.

2-Benzyl-9-(trifluoromethoxy)-1,2,3,10*b*-tetrahydrobenzo[*e*]imidazo[1,5-*c*][1,2,3] oxathiazine 5,5-dioxide (3fa): Pale yellow oil; Yield 80% (64 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.30–7.38 (m, 3H), 7.18–7.28 (m, 3H), 7.09–7.15 (m, 1H), 6.96 (d, J = 3 Hz, 1H),

5.16 (dd, *J* = 6.5, 4.3 Hz, 1H), 4.44 (d, *J* = 7.3 Hz, 1H), 4.23 (d, *J* = 7.2 Hz, 1H), 3.77 (s, 2H), 3.45–3.53 (m, 1H), 3.22 (dd, *J* = 11.0, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.8, 146.2, 146.1, 136.9, 128.7, 128.5, 127.9, 124.4, 122.0, 120.6, 120.4 (*J* = 240 Hz), 119.2, 72.2, 61.2, 60.0, 57.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{16}F_3N_2O_4S$ 401.0783; Found 401.0792; IR (Neat): 2923, 2843, 1490, 1403 cm^{-1}.

2-Benzyl-9-nitro-1,2,3,10*b*-tetrahydrobenzo[*e*]imidazo [1,5-*c*][1,2,3]oxathiazine 5,5-dioxide (3ga): Pale yellow oil; Yield 68% (49 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (dd, *J* = 8.9, 2.4 Hz, 1H), 8.05 (d, *J* = 2.8 Hz, 1H), 7.37–7.31 (m, 4H), 7.26–7.22 (m, 2H), 5.25 (dd, *J* = 6.3, 3.8 Hz, 1H), 4.46 (d, *J* = 7.0 Hz, 1H), 4.18 (d, *J* = 7.0 Hz, 1H), 3.77 (q, *J* = 13.1 Hz, 2H), 3.54 (dd, *J* = 10.9, 6.4 Hz, 1H), 3.29 (dd, *J* = 10.9, 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3, 155.1, 144.9, 136.5, 128.8, 128.5, 128.1, 128.0, 124.7, 122.4, 120.3, 72.0, 61.3, 60.2, 57.6; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{16}N_3O_5S$ 362.0811; Found 362.0809; IR (Neat): 2959, 2833, 1463, 1275 cm^{-1}.

1-Benzyl-4-methyl-1*H*-benzo[*c*][1,2,6]thiadiazine 2,2-dioxide (4b): Following a reported procedure,[18] **4a** was prepared. In the substrate **4a**, benzyl bromide (1.2 equiv, 0.5 mmol), triethylamine (1.2 equiv, 0.6 mmol) and THF (2 mL) were added and heated at 60 ^{o}C for 4 h. The reaction mixture was diluted with ethyl acetate (10 mL), extracted with water (2 x 5 mL). The organic layer was concentrated under vacuum and purified by column chromatography (100-200# Silica). Yellow solid; 64% Yield (91 mg); mp 183-185 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.54 (ddd, *J* = 8.6, 7.2, 1.5 Hz, 1H), 7.45–7.40 (m, 2H), 7.39–7.33 (m, 2H), 7.33–7.27 (m, 1H), 7.20–7.15 (m, 1H), 7.12–7.08 (m, 1H), 5.24 (s, 2H), 2.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.8, 142.5, 135.7, 135.3, 129.3, 129.0, 127.9, 126.9, 122.3,

118.6, 116.7, 49.7, 24.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{15}N_2O_2S$ 287.0854; Found 287.0860.

6-Chloro-4-phenyl-1*H*-benzo[*c*][1,2,6]thiadiazine 2,2-dioxide (4c′): Following the reported procedure,[18] **4c′** was prepared from (2-amino-5-chlorophenyl)(phenyl) methanone as a substrate. After reaction, the crude was purified by column chromatography (100-200#) using Hexane and EtOAc to obtain the desired cyclic sulfonylimine as yellow sticky solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73–7.68 (m, 2H), 7.68–7.64 (m, 1H), 7.60–7.52 (m, 4H), 7.22 (d, J = 8.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 140.7, 135.8, 134.7, 132.4, 130.8, 130.5, 128.8, 128.0, 119.9, 117.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{10}ClN_2O_2S$ 293.0152; Found 293.0157.

1-Benzyl-6-chloro-4-phenyl-1*H*-benzo[*c*][1,2,6] thiadiazine 2,2-dioxide (4c): To the substrate **4c′**, benzyl bromide (1.2 equiv) and triethylamine (1.2 equiv) in THF (2 mL) were added, and the mixture was heated at 60 ^{o}C for 4 h. The reaction mixture was diluted with ethyl acetate (10 mL) and extracted with water (2 x 5 mL). The organic layer was concentrated under vacuum and purified by column chromatography (100-200# Silica). Yellow solid; 64% Yield (91 mg); mp 121-123 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74–7.68 (m, 2H), 7.66 (td, J = 7.5, 1.6 Hz, 1H), 7.63–7.52 (m, 4H), 7.44–7.40 (m, 2H), 7.40–7.34 (m, 2H), 7.34–7.30 (m, 1H), 7.20 (d, J = 9.0 Hz, 1H), 5.29 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 142.3, 135.5, 135.0, 132.5, 131.3, 130.8, 129.1, 128.8, 128.2, 127.9, 127.0, 120.0, 118.9, 50.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{16}ClN_2O_2S$ 383.0621; Found 383.0630.

2,6-Dibenzyl-10*b*-methyl-2,3,6,10*b*-tetrahydro-1*H*-benzo[*d*]imidazo[1,5-*b*][1,2,6]thiadiazine 5,5-dioxide (5ba): Yellow solid; Yield 60% (50 mg); mp. 121-123 ^{o}C; ^{1}H NMR (400 MHz,

$CDCl_3$): δ 7.34–7.30 (m, 2H), 7.27–7.20 (m, 6H), 7.12–7.08 (m, 2H), 7.05–6.99 (m, 2H), 6.96–6.90 (m, 1H), 6.69–6.64 (m, 1H), 5.09 (d, J = 17.1 Hz, 1H), 4.79 (d, J = 17.1 Hz, 1H), 4.30 (d, J = 6.8 Hz, 1H), 4.05 (d, J = 6.8 Hz, 1H), 3.62 (d, J = 13.3 Hz, 1H), 3.54 (d, J = 13.1 Hz, 1H), 3.25 (d, J = 9.8 Hz, 1H), 2.98 (d, J = 10.0 Hz, 1H), 1.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.1, 137.5, 136.8, 128.8, 128.5, 128.4, 128.1, 127.7, 127.5, 127.4, 126.7, 126.5, 125.6, 122.9, 116.6, 72.8, 69.9, 69.1, 57.5, 49.2, 28.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{26}N_3O_2S$ 420.1746; Found 420.1742; IR (KBr): 3028, 2927, 2857, 1487, 1179 cm^{-1}.

2,6-Dibenzyl-9-chloro-10*b*-phenyl-2,3,6,10*b*-tetrahydro-1*H*-benzo[d]imidazo[1,5-*b*][1,2,6]thiadiazine 5,5-dioxide (5ca): Yellow semi-solid; Yield 54% (55 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55−7.51 (m, 2H), 7.38−7.29 (m, 8H), 7.28–7.24 (m, 3H), 7.22−7.19 (m, 3H), 7.17–7.16 (m, 1H), 6.83 (d, J = 8.5 Hz, 1H), 5.04 (d, J = 16.6 Hz, 1H), 4.84 (d, J = 16.6 Hz, 1H), 4.48−4.39 (m, 2H), 3.72 (d, J = 3.0 Hz, 2H), 3.56−3.49 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.5, 137.9, 137.2, 136.0, 128.8, 128.7, 128.6, 128.5, 128.4, 128.1, 128.0, 128.0, 127.7, 127.7, 127.5, 126.9, 119.9, 73.6, 72.2, 68.9, 57.4, 49.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{27}ClN_3O_2S$ 516.1513; Found 516.1521; IR (KBr): 3029, 2924, 2853, 1483, 1370, 1174 cm^{-1}.

2-((*S*)-1-Phenylethyl)-1,2,3,10*b*-tetrahydrobenzo[*e*] imidazo[1,5-*c*][1,2,3]oxathiazine 5,5-dioxide (6de): Transparent sticky oil; Yield 83% (diastereomeric ratio 1:1, 55 mg); 1st diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.36 (m, 4H), 7.14–7.23 (m, 3H), 7.07 (dd, J = 7.8, 0.8 Hz, 1 H), 6.95–7.02 (m, 1H), 5.10 (dd, J = 6.1, 3.4 Hz, 1 H), 4.53 (d, J = 6.5 Hz, 1H), 4.18 (d, J = 6.3 Hz, 1H), 3.51 (q, J = 6.5 Hz, 1H), 3.24 (dd, J = 10.3, 6.0 Hz, 1H), 3.03 (dd, J = 10.3, 4.0 Hz, 1H), 1.35 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.9, 143.6, 129.0,

128.7, 127.6, 126.9, 126.1, 125.7, 122.6, 118.9, 70.2, 62.0, 61.0, 60.1, 22.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{19}N_2O_3S$ 331.1116; Found 331.1123; IR (Neat): 2925, 2852, 1454, 1399, 1190 cm^{-1}. 2nd diastereomer: ^1H NMR (400 MHz, $CDCl_3$): δ 7.31–7.38 (m, 2H), 7.27–7.31 (m, 2H), 7.20–7.26 (m, 3H), 7.09–7.13 (m, 1H), 7.07 (dd, *J* = 7.9, 0.8 Hz, 1H), 5.17 (dd, *J* = 6.4, 3.4 Hz, 1H), 4.28 (d, *J* = 6.8 Hz, 1H), 4.06 (d, *J* = 6.8 Hz, 1H), 3.48 (q, *J* = 6.5 Hz, 1 H), 3.41 (dd, *J* = 10.2, 3.4 Hz, 1H), 3.25 (dd, *J* = 10.2, 3.4 Hz, 1H), 1.37 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.8, 143.3, 129.1, 128.7, 127.7, 126.9, 126.4, 125.8, 122.8, 119.1, 70.8, 62.1, 61.2, 59.6, 22.8.

2-Phenethyl-1,2,3,10*b*-tetrahydrobenzo[*e*]imidazo[1,5-*c*][1,2,3]oxathiazine 5,5-dioxide (6df): Light yellow oil; Yield 72% (48 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.36−7.21 (m, 5H), 7.17−7.13 (m, 2H), 7.13−7.09 (m, 1H), 7.06 (dd, *J* = 1.3, 8.3 Hz, 1H), 5.13 (dd, *J* = 4.0, 6.3 Hz, 1H), 4.47 (d, *J* = 7.0 Hz, 1H), 4.19−4.16 (m, 1H), 3.49−3.42 (m, 1H), 3.26 (dd, *J* = 4.0, 10.8 Hz, 1H), 282–2.76 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.7, 139.1, 129.1, 128.6, 128.5, 126.4, 126.4, 125.9, 122.7, 119.1, 72.3, 62.0, 60.3, 55.5, 35.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{19}N_2O_3S$ 331.1116; Found 331.1119; IR (Neat): 2959, 2930, 2873, 1454, 1287 cm^{-1}.

10*b*-Methyl-2-phenethyl-1,2,3,10*b*-tetrahydrobenzo[*e*] imidazo[1,5-*c*][1,2,3]oxathiazine 5,5-dioxide (6af):Pale yellow oil; Yield 83% (57 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.35−7.30 (m, 1H), 7.28−7.19 (m, 5H), 7.11−7.07 (m, 2H), 7.04 (dd, *J* = 8.0, 1.3 Hz, 1H), 4.53 (d, *J* = 6.8 Hz, 1H), 4.12 (d, *J* = 6.8 Hz, 1H), 3.38 (d, *J* = 9.8 Hz, 1H), 3.05 (d, *J* = 10.0 Hz, 1H), 2.78−2.64 (m, 4H), 1.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.0, 139.2, 129.1, 128.6, 128.4, 127.4, 126.5, 126.3, 125.9, 119.0, 72.8, 69.4, 69.2, 54.9, 35.1, 27.2; HRMS (ESI-TOF) m/z: $[M + H]^+$

Calcd for $C_{18}H_{21}N_2O_3S$ 345.1273; Found 345.1277; IR (Neat): 2959, 2853, 1400, 1283, 1178 cm^{-1}.

4-((Benzylamino)methyl)-7-methoxy-3,4-dihydro benzo[e][1,2,3]oxathiazine 2,2-dioxide (7a): Yellow solid; 93% Yield (62 mg); mp 139-141 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 7.39–7.29 (m, 3H), 7.27–7.22 (m, 2H), 7.07 (d, J = 8.8 Hz, 1H), 6.77 (dd, J = 8.7, 2.6 Hz, 1H), 6.56 (d, J = 2.5 Hz, 1H), 4.84 (m, 1H), 3.81 (s, 3H), 3.78 (s, 2H), 3.45 (dd, J = 12.7, 3.9 Hz, 1H), 3.03 (dd, J = 3.8, 12.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.4, 152.9, 138.8, 128.7, 128.1, 127.6, 126.4, 112.5, 111.6, 103.9, 55.8, 55.6, 53.5, 49.8; HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{19}N_2O_4S$ 335.1066; Found 335.1063; IR (KBr): 3404, 2923, 2852, 1626, 1506, 1456, 1377, 1188 cm^{-1}.

4-(((3-Methoxybenzyl)amino)methyl)-4-methyl-3,4-dihydrobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (7b): Yellow solid; 97% Yield (67 mg); mp 108-110 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 7.35–7.17 (m, 4H), 7.04 (dd, J = 8.2, 1.1 Hz, 1H), 6.86–6.81 (m, 1H), 6.78 (d, J = 7.5 Hz, 1H), 6.74 (d, J = 2.0 Hz, 1H), 3.82 (s, 3H), 3.67 (s, 2H), 3.30 (d, J = 12.5 Hz, 1H), 2.70 (d, J = 12.5 Hz, 1H), 1.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 151.2, 140.6, 129.7, 129.7, 126.1, 125.8, 124.6, 120.2, 119.5, 113.5, 112.9, 62.3, 58.2, 55.2, 53.2, 27.3; HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{21}N_2O_4S$ 349.1222; Found 349.1226; IR (KBr): 3417, 2960, 2930, 2873, 1726, 1582, 1448, 1378, 1286 cm^{-1}.

2-(1-Amino-2-(benzyl(methyl)amino)ethyl)phenol (7c): Pale yellow oil; Yield 97% (30 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.41–7.30 (m, 5H), 7.20–7.13 (m, 1H), 6.95 (dd, J = 7.4, 1.4 Hz, 1H), 6.88–6.76 (m, 2H), 4.24 (dd, J = 11.4, 3.6 Hz, 1H), 3.74–3.62 (m, 1H), 3.62–3.53 (m, 1H), 2.90 (t, J = 11.9 Hz, 1H), 2.43 (dd, J = 12.7, 3.6 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 129.1, 128.6, 128.4, 127.9, 127.3, 125.2, 118.9, 117.3, 62.4, 53.6, 41.9, 29.7;

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{21}N_2O$ 257.1654; Found 257.1656; IR (Neat): 3547, 2925, 2855, 1612, 1514, 1456, 1159 cm^{-1}.

2-(3-Methoxybenzyl)-9*b*-phenyl-1,2,3,9*b*-tetrahydrobenzo[*d*]imidazo[1,5-*b*]isothiazole 5,5-dioxide (9ad): Transparent oil; 73% Yield (59 mg); ^1H NMR (400 MHz, $CDCl_3$):δ 8.05–8.03 (m, 1 H), 8.00–7.98 (m, 2H), 7.83–7.75 (m, 4H), 7.53–7.48 (m, 2H), 7.21–7.17 (m, 1H), 6.80−6.78 (m, 1H), 6.72−6.70 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 143.8, 142.3, 138.9, 134.9, 129.5, 129.3, 129.2, 128.9, 127.9, 126.6, 125.6, 123.1, 121.4, 113.3, 71.3, 65.9, 60.4, 56.4, 55.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{23}N_2O_3S$ 407.1429; Found 407.1437; IR (Neat): 2926, 2839, 1624, 1400, 1196 cm^{-1}.

2-Phenethyl-9*b*-phenyl-1,2,3,9*b*-tetrahydrobenzo[*d*]imidazo[1,5-*b*]isothiazole 5,5-dioxide (9af): Transparent oil; Yield 78% (60 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.75 (dd, J = 7.7 Hz, 1H), 7.72–7.67 (m, 2H), 7.62–7.56 (m, 1H), 7.55–7.46 (m, 2H), 7.43–7.37 (m, 2H), 7.34–7.29 (m, 1H), 7.2–7.23 (m, 2H), 7.23–7.18 (m, 1H), 7.14–7.09 (m, 2H), 5.05 (d, J = 9.3 Hz, 1H), 4.00–3.91 (m, 1H), 3.82 (d, J= 8.8 Hz, 1H), 3.27 (d, J = 9.8 Hz, 1H), 2.83–2.54 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.7, 142.3, 139.4, 134.8, 133.6, 129.4, 129.0, 128.7, 128.4, 128.0, 126.3, 125.6, 123.9, 121.4, 71.3, 66.9, 54.4, 35.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{23}N_2O_2S$ 391.1480; Found 391.1483; IR (Neat): 2957, 2927, 2879, 1455, 1286 cm^{-1}.

ASSOCIATED CONTENT

Supporting Information

Copies of ^1H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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