Md. Rafiqul Islam,[a] Yuji Takikawa,[b] and Kwon Taek Lim[a]*

[a]Department of Imaging System Engineering, Pukyong National University, Busan, 608-737, South Korea
[b]Department of Chemistry and Bioengineering, Iwate University, Morioka, Iwate 020-8551, Japan
*E-mail: ktlim@pknu.ac.kr

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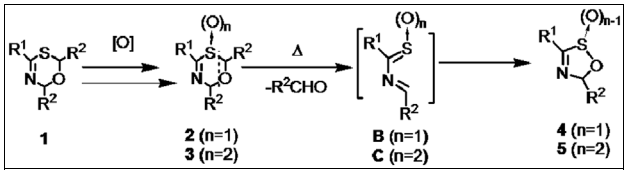

A series of novel 6*H*-1,3,5-oxathiazine *S,S*-dioxides were synthesized by the *m*-CPBA oxidation (2.2 equiv) of 6*H*-1,3,5-oxathizines. The synthetic utilities of the newly synthesized cyclic sulfones were investigated. In a thermal condition, compounds 6*H*-1,3,5-oxathiazine *S,S*-dioxides were found relatively stable, but Lewis acid-induced thermal reaction afforded the corresponding amides. The plausible pathway to amides from 6*H*-1,3,5-oxathiazine *S,S*-dioxides was also discussed in this account.

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INTRODUCTION

The interest in synthesizing heterocycles has always been enormous because the majority of pharmaceuticals and biologically active chemicals are heterocyclic in nature. Among heterocycles, the six and five-membered *O*-, *S*-, and *N*-heterocycles are probably the most common structural motifs spread across natural products [1,2]. Sulfones are a major class of organosulfur compounds that have been extensively used as versatile intermediates in organic synthesis [3]. The importance of the sulfone functional group in synthetic organic chemistry warrants significant interest in the development of new methodologies related to the introduction of the sulfone functionality into an organic molecule as well as the further synthetic transformation of the sulfone intermediate, and, when desirable and possible, its eventual elimination from the target [4,5]. Cyclic sulfones, in particular, have unique synthetic utilities. For example, cyclic sulfones have been investigated as the key subunit and scaffold for the construction of biologically active molecules [6].

On the other hand, a great interest has been focused on the generation and synthetic application of thione *S*-oxides (sulfine), thione *S,S*-dioxides (sulfene), and their thio analogs because of their multifunctional reactivities for the synthesis of useful heterocyclic compounds [7,8]. However, only a very few studies on the framework of heterodienes conjugated with a sulfine or sulfene have been carried out because of the lack of methods for the synthesis of their precursors [9–12]. Our strategy is to generate such highly reactive intermediates (Fig. 1) through thermal cycloreversion of appropriate heterocyclic precursors as shown in Scheme 1.

In this way, we already have developed a novel method for generating 1,3-thiaza-1,3-butadiene *S*-oxides (sulfine) **B** for the synthesis of 5*H*-1,2,4-oxathiazoles **4** by thermal cycloreversion of 6*H*-1,3,5-oxathiazine *S*-oxides **2** [13,14]. These findings encouraged us to expand the scope leading to their higher oxidized variants α,β-unsaturated heterodiene **C** by thermal cycloreversion of 6*H*-1,3,5-oxathiazine *S,S*-dioxides **3**. The big challenge was to synthesize the precursor **3**. Although, a plethora of methods for the synthesis of cyclic sulfones exists in the literature [3], but a generally applicable and highly efficient approach to the synthesis of cyclic sulfones having nitrogen and chalcogen functionalities of various substitution patterns is still highly desirable. The majority of existing methodologies for the synthesis of cyclic sulfones involve the construction of the corresponding cyclic sulfides from appropriately functionalized precursors, followed by oxidation of the sulfides to sulfones.

In this article, we describe a facile and convenient method for the synthesis of cyclic sulfones **3** on the basis of *m*-CPBA oxidation of **2**. In addition, synthetic utilities of the new compounds **3** have also been encompassed in this report.

RESULTS AND DISCUSSION

Synthesis of 6*H*-1,3,5-oxathiazine *S,S*-dioxides 3. 6*H*-1,3,5-Oxathiazines **1** were prepared by treating an aryl thioamide with an aliphatic aldehyde and $BF_3.OEt_2$ according to the reported procedures [15–17]. We found that treatment of **1** with 1.1 equiv of *m*-CPBA at 0 °C for 1 h afforded **2** in quantitative yield [14]. Accordingly, we took an attempt to synthesize **3** by two step successive oxidation of **1** using 1.1 equiv *m*-CPBA, but in contrast to our expectation, we have 5*H*-1,2,4-oxathiazole *S*-oxide **5** in quantitative yield instead of desired **3**. On the other hand, when the $CHCl_3$

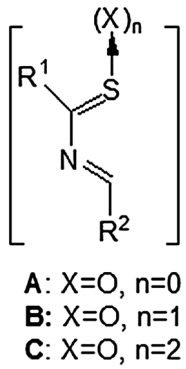


Figure 1. Reactive building blocks.

solutions of **1a–d** were treated with 2.2 equiv of *m*-CPBA at 0 °C for 1 h, the corresponding 6*H*-1,3,5-oxathizine *S,S*-dioxides **3a–d** were obtained as single epimer in quantitative yields. However, the *m*-CPBA (2.2 equiv) oxidation of **1e–f** (bearing a methyl or iso-propyl group at the C-2 and C-6 positions) afforded complex mixtures. The physical data of **3a–d** were fully consistent with their assigned structures. The stereoselective formation of **3a–d** might be occurred because of the presence of a bulky *t*-butyl substituent at the C-2 and C-6 positions of **1a–d**. All results concerning 2.2 equiv *m*-CPBA oxidation of **1a–f** are shown in Table 1.

Reactivity of 6*H*-1,3,5-oxathiazine *S*,*S*-dioxides 3. It was observed that toluene solutions of compounds **3** were much stable toward heating. When **3a** was heated in toluene refluxing temperature for 72 h, only a trace of benzamide **6a** was formed along with recovery (Table 2, run 2). However, the neat compound **3a** gave a complex mixture when standing it at room temperature for around 12 h. On the other hand, when toluene solutions of compounds **3** were treated with silica gel at refluxing temperature, the corresponding amides **6** were afforded in moderate yields (Table 2, run 3–6). However, the treatment of **3d** with silica gel afforded nitriles **7d** as a minor product along with **6d** (Table 2, run 6). The formation of **7d** could be explained by the fact that the push–pull type substituent effect of the electron-donating substituent, *p*-methoxyphenyl group, might accelerate the C-S bond cleavage to afford **7d**. The similar result was also observed when the toluene solution of **3d** was treated with *p*-toluene sulfonic acid (Table 2, run 7). Attempts were undertaken to trap the plausible sulfene **C** using standard trapping agents such as dimethyl acetylenedicarboxylate and EtOH, but no effort was successful.

Reactivity of 5*H*-1,2,4-oxathiazole *S*-oxides 5. 5*H*-1,2,4-Oxathiazole *S*-oxides **5** were synthesized by *m*-CPBA (1.1 equiv) oxidation of 5*H*-1,2,4-oxathiazole **4** that was obtained through thermal cycloreversion of 6*H*-1,3,5-oxathiazniene *S*-oxides **2**. The thermal stability and reactivities of compounds **5** were closely examined. The neat **5a** was observed almost to be unchanged even storing for 3 months at ambient condition. When a $CDCl_3$ solution of **5a** was monitored by ^{1}H NMR for 720 h (a month) and 1440 h (2 months) at room temperature, a very slow conversion of **5a** was recorded with a major recovery. Moreover, when a $CHCl_3$ solution of **5a** was heated in refluxing temperature, then, 11% of **6a** was afforded within 24 h along with recovery (Table 3, run 4). Treatment of **5a** with silica gel (2 equiv) in $CHCl_3$ at room temperature for 168 h gave 9% of **6a** along with 83% recovery and some other unidentified compounds. In contrast, when **5** was heated with 2.0 equiv of silica gel (Lewis acid) in the chloroform refluxing temperature for 24 h, it resulted moderate yield of **6** (Table 3, runs 6–10). However, the comparable yields were afforded when the aforementioned reactions were carried out at toluene refluxing temperature for 2 h (Table 3, runs 11–15). In the ^{1}H NMR spectrum of the aforementioned crude products, we did not observe any peak responsible for 3,5-diphenyl-1,2,4-thidiazole **8**, that was the main product of **4** with silica gel [14]. These results suggest that at high temperature, the compound **5** does not give any deoxygenated product **4**. When **5** having an aryl group with an electron-donating moiety in the C-3 position was reacted with silica gel or *p*-TsOH, then, the corresponding nitriles **7** was formed along with amides **6** (Table 3, runs 9, 10, 14, and 15). It is speculated that Lewis acid-induced fragmentation of **5** afforded thioamide-*S*-oxides that upon extrusion of sulfur subsequently leads to **6**; on the other hand, nitriles **7** might be afforded by C-S bond fission of **5** because of the push–pull nature of the electron-donating group.

Plausible formation pathway of amide 6 from **1**. The two step successive oxidation of 6*H*-1,3,5-oxathizine **1** by 1.1 equiv *m*-CPBA afforded 5*H*-1,2,4-oxathiazole *S*-oxides **5**, which could be explained in the way that in the first step of oxidation **2** was formed, which underwent thermal

Scheme 1. A plausible approach for the generation of sulfine and sulfene building blocks.

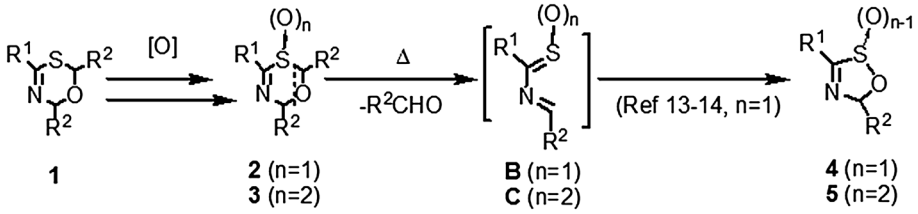
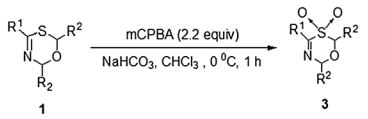


Table 1

Synthesis of 6*H*-1,3,5-oxathiazine *S*,*S*-dioxides **3**.



1 3

Entry	Substrate R^1	Substrate R^2	1	Yield (%)[a] 3
1	C_6H_5	*t*-Bu	**1a**	65
2	*p*-ClC_6H_4	*t*-Bu	**1b**	61
3	*p*-FC_6H_4	*t*-Bu	**1c**	69
4	*p*-$MeOC_6H_4$	*t*-Bu	**1d**	52
5	C_6H_5	*i*-Pr	**1e**	—[b]
6	C_6H_5	Me	**1f**	—[b]

[a]Isolated yield.
[b]Complex mixture.

cycloreversion to afford **4** via generation of sulfine **B**, the subsequent *m*-CPBA (1.1 equiv) oxidation of **4** resulted in **5** in quantitative yield [14]. On the other hand, when **5** was heated for a long time, or kept standing at room temperature for a prolonged period or treated with silica gel (Lewis acid) for a long time, then, **6** was afforded in a good yield. In the similar manner, the Lewis acid-induced thermal reaction of **3** also gave **6** in a moderate yield. These results suggest that heating of **3** initially affords **5** via most likely 1,3-thiaza-1,3-butadiene *S*,*S*-dioxides **C**, and subsequently, the Lewis acid mediated fragmentation of **5** gives **6** (Scheme 2). However, attempts for trapping of the highly reactive intermediates **C** were not successful. The detailed mechanistic study is yet to be explored.

CONCLUSION

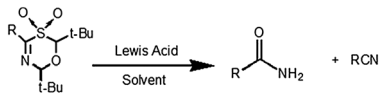
A number of 6*H*-1,3,5-oxathiazine *S,S*-dioxides **3** were successfully synthesized by a simple 2.2 equiv *m*-CPBA oxidation of 6*H*-1,3,5-oxathizines **1**. The thermal reaction of **3** afforded **6** in a good yield. On the other hand, the thermolysis of 3*H*-1,2,4-oxathizole *S*-oxides **5** also gave **6** in a moderate yield. With the available findings into account, it can be speculated that thermal retro-[4 + 2] cycloreversion of **3** afforded **5** via transiently generation and facile ring closure of 1,3-thiaza-1,3-butadiene *S*,*S*-dioxide **C**, and then, Lewis acid-induced fragmentation of **5** subsequently gave **6**.

EXPERIMENTAL

General. Melting points were measured in open capillary tubes with a Buchi 535 micro-melting point apparatus (BUCHI Labortechnik AG, Flawil, Switzerland) and are uncorrected. ^{1}H NMR spectra were determined at 400 MHz (Bruker AC-400P spectrometer, Billerica, MA)), and ^{13}C NMR spectra were determined at 100 MHz (Bruker AC-400P spectrometer, Billerica, Massachusetts). Chemical shifts are expressed in parts per million (δ units) downfield from TMS used as an internal reference. Mass spectra were recorded on a Hitachi M-2000 mass spectrometer (Tokyo, Japan) with electron-impact ionization at 20 or 70 eV using a direct inlet system. IR spectra were recorded for thin film (neat) or KBr disks on a JASCO FT/IR-7300 spectrometer (Tokyo, Japan). Elemental analyses were performed using a Yanagimoto CHN (Carbon, Hydrogen,

Table 2

Reactivity of 5*H*-1,3,5-oxathizine *S*,*S*-dioxides **3**.



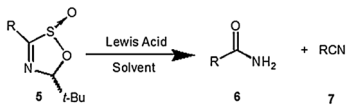
3 6 7

Entry	Substrates R	3	Lewis acid (equiv)	Solvent	Temp. (°C)	Time (h)	Yield (%)[a] 6	7	Recovery
1	C_6H_5	**3a**	None	None	RT	12	—[b]	—[b]	—[b]
2	C_6H_5	**3a**	None	Toluene	Reflux	72	Trace	0	Quantitative
3	C_6H_5	**3a**	Silica gel (2.0)	Toluene	Reflux	12	47	0	—
4	*p*-ClC_6H_4	**3b**	Silica gel (2.0)	Toluene	Reflux	12	58	0	—
5	*p*-FC_6H_4	**3c**	Silica gel (2.0)	Toluene	Reflux	12	61	0	—
6	*p*-$MeOC_6H_4$	**3d**	Silica gel (2.0)	Toluene	Reflux	12	53	11	—
7	*p*-$MeOC_6H_4$	**3d**	*p*-TsOH (2.0)	Toluene	Reflux	4	59	12	—

[a]Isolated yield.
[b]Complex mixture.
[c]Yield was estimated by ^{1}H NMR.

Table 3

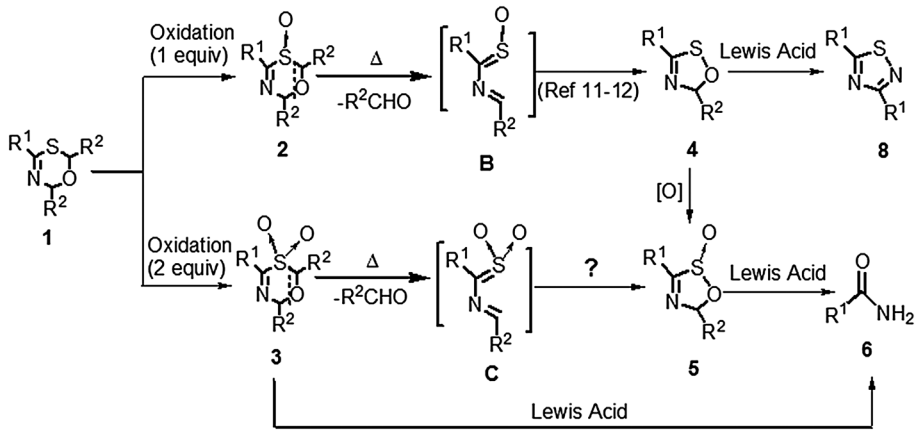
Reactivity of 5*H*-1,2,4-oxathiazole *S*-oxides **5**.



Entry	Substrates		Lewis acid (2.0 equiv)	Solvent	Temp (°C)	Time (h)	Yield (%)[a]		
	R	**5**					**6**	**7**	(Recovery)
1	C_6H_5	**5a**	None	None	RT	168	0	0	Quantitative
2	C_6H_5	**5a**	DCl[b]	$CDCl_3$	RT	720	3	0	94[c]
3	C_6H_5	**5a**	DCl[b]	$CDCl_3$	RT	1440	7	0	87[c]
4	C_6H_5	**5a**	HCl[b]	$CHCl_3$	Reflux	24	11	0	76
5	C_6H_5	**5a**	Silica gel	$CHCl_3$	RT	168	9	0	83
6	C_6H_5	**5a**	Silica gel	$CHCl_3$	Reflux	24	61	0	—
7	*p*-ClC_6H_4	**5b**	Silica gel	$CHCl_3$	Reflux	168	69	0	—
8	*p*-FC_6H_4	**5c**	Silica gel	$CHCl_3$	Reflux	24	71	0	—
9	*p*-$MeOC_6H_4$	**5d**	Silica gel	$CHCl_3$	Reflux	168	65	14	—
10	*p*-$MeOC_6H_4$	**5d**	*p*-TsOH	$CHCl_3$	Reflux	24	69	16	—
11	C_6H_5	**5a**	Silica gel	Toluene	Reflux	24	52	0	—
12	*p*-ClC_6H_4	**5b**	Silica gel	Toluene	Reflux	24	63	0	—
13	*p*-FC_6H_4	**5c**	Silica gel	Toluene	Reflux	24	65	0	—
14	*p*-$MeOC_6H_4$	**5d**	Silica gel	Toluene	Reflux	24	61	12	—
15	*p*-$MeOC_6H_4$	**5d**	*p*-TsOH	Toluene	Reflux	2	67	15	—

[a]Isolated yield.
[b]It was assumed that DCl/HCl was generated through the decomposition of $CDCl_3$/$CHCL_3$.
[c]Yield was estimated by ^{1}H NMR.

Scheme 2. The probable pathway for the conversion of **1** into **6** via compound **3**.



Nitrogen) recorder MT-5 (Yanagimoto Mfg. Co., Kyoto, Japan). Column chromatography was performed using silica gel (Merck, Cat. No. 7734) without pretreatment. All substrates and reagents were commercially available reagent grade and were used without further pretreatment.

General procedure for the preparation of 2,4,6-trisubstituted 6*H*-1,3,5-oxathiazines (1). A 20 mL chloroform solution of alkanethioamide or an arenethioamide (10.0 mmol) was treated with 2,4,6-trimethyl-1,3,5-trioxane (1.04 g, 8.00 mmol), pivalaldehyde (2.06 g, 24.0 mmol), or isobutyraldehyde (1.73 g, 24.0 mmol) and $BF_3{\cdot}OEt_2$ (2.84 g, 20 mmol) at 0 °C, and the reaction mixture was stirred for 4–5 h at room temperature. The reaction mixture was then quenched with an aqueous $NaHCO_3$ solution and was extracted with chloroform. The organic layer was washed with water and was dried over anhydrous Na_2SO_4. After removing the solvent in vacuo, the crude product was purified using column chromatography on silica gel to afford 2,6-dialkyl-4-aryl-6*H*-1,3,5-oxathiazine or 2,4,6-trialkyl-6*H*-1,3,5-oxathiazine (**1**) in good yields. Further purification of solidified products was carried out by recrystallization using hexane.

2,6-Di-tert-butyl-4-phenyl-6H-1,3,5-oxathiazine (1a). Colorless plates, mp 95.2–95.8 °C (Lit. [14], 95.4–96.0 °C).

2,6-Di-tert-butyl-4-(p-chlorophenyl)-6H-1,3,5-oxathiazine (1b). Colorless crystals, mp 95.5–96.1 °C (decomp.) (Lit. [14], 95.4–96.0 °C decomp.).

2,6-Di-tert-butyl-4-(p-fluorophenyl)-6H-1,3,5-oxathiazine (1c). Colorless plates, mp 55.4–56.6 °C (decomp.) (Lit. [14], 55.5–56.5 °C decomp.).

2,6-Di-tert-butyl-4-(p-methoxyphenyl)-6H-1,3,5-oxathiazine (1d). Colorless needles, mp 101.2 °C; (Lit. [14], 101 °C decomp.).

2,6-Diisopropyl-4-phenyl-6H-1,3,5-oxathiazine (1e). Pale yellow oil, (Lit. [14]); ^{1}H NMR ($CDCl_3$): δ 1.04 (6H, dd, J = 6.2, 6.1 Hz), 1.09 (6H, dd, J = 6.3, 6.2 Hz), 2.06 (1H, quint, J = 6.5 Hz), 2.17 (1H, quint, J = 6.5 Hz), 5.00 (1H, d, J = 1.5 Hz), 5.02 (1H, d, J = 2.5 Hz), 7.36–7.42 (3H, m), 7.82–7.84 (2H, m).

2,6-Dimethyl-4-phenyl-6H-1,3,5-oxathiazine (1f). Pale yellow oil, (Lit. [14]); ^{1}H NMR ($CDCl_3$): δ 1.61 (3H, d, J = 6.1 Hz), 1.62 (3H, d, J = 6.2 Hz), 5.28 (1H, q, J = 6.2 Hz), 5.36 (1H, q, J = 6.1 Hz), 7.35–7.43 (3H, m), 7.78–7.81 (2H, m).

Preparation of 2,4,6-trisubstituted 6*H*-1,3,5-oxathiazine *S,S*-dioxides (3) by *m*-CPBA oxidation of 6*H*-1,3,5-oxathiazines (1). A chloroform solution (20 mL) of 6*H*-1,3,5-oxathiazine (**1**, 1.0 mmol) was treated with *m*-CPBA (2.2 equiv) at 0 °C in the presence of $NaHCO_3$ (2 equiv). The reaction mixture was quenched with aqueous Na_2SO_3 solution and was extracted with chloroform. The mixture was then subjected to the usual work-up. After removing the solvent in vacuo, the products **3** were purified by the silica gel chromatography in moderate yield as single epimers (**3a–d**).

2,6-Di-tert-butyl-4-phenyl-6H-[1,3,5]oxathiazine S,S-dioxide (3a). Colorless needles; mp 135–137 °C (decomp.); MS *m/z* 238 ($M^+ - t$BuCHO + 1; 6%), 70 ($M^+ - C_6H_5CN - t$BuCHO − SO_2; 100%); IR (KBr): 2977, 1661, 1625, 1478, 1364, 1309, 1201, 1131, 1093, 1062, 999, 766 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.10 (9H, s), 1.25 (9H, s), 4.48 (1H, s), 4.83 (1H, s), 7.38–7.53 (3H, m), 8.01–8.04 (2H, m); ^{13}C NMR ($CDCl_3$): δ 25.3 (q), 25.9 (q), 36.3 (s), 37.3 (s), 98.2 (d), 98.4 (d), 128.4 (d), 128.5 (d), 129.7 (s), 131.7 (d), 158.8 (s); Calcd for $C_{17}H_{25}NO_3S$: C, 63.13; H, 7.79; N, 4.33%; Found: C, 63.22; H, 7.81; N, 4.36%.

2,6-Di-tert-butyl-4-(4-chlorophenyl)-6H-[1,3,5]oxathiazine S, S-dioxide (3b). Colorless needles; mp 135–137 °C (decomp.); MS *m/z* 155 ($M^+ - ClC_6H_4CN$-$SO_2 - 1$; 63%), 139 ($M^+ - t$Bu-CHO − SO_2-tBuCH + 2; 100%); IR (KBr) 2977, 1622, 1489, 1306, 1134, 1095 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.09 (9H, s), 1.25 (9H, s), 4.48 (1H, s), 4.83 (1H, s), 7.41 (2H, d, J = 6.8 Hz), 8.00 (2H, d, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 25.3 (q), 25.9 (q), 36.3 (s), 37.3 (s), 98.4 (d), 98.5 (d), 128.1 (s), 128.9 (d), 129.7 (d), 158.0 (s), 170.3 (s); Calcd for $C_{17}H_{24}ClNO_3S$: C, 57.05; H, 6.76; N, 3.91%; Found: C, 57.21; H, 6.79; N, 3.96%.

2,6-Di-tert-butyl-4-(4-fluorophenyl)-6H-[1,3,5]oxathiazine S, S-dioxide (3c). Colorless needles; mp 143–145 °C (decomp.); MS *m/z* 325 ($M^+ - O$; 5%), 204 ($M^+ - FC_6H_4CNO$; 100%); IR (KBr) 2977, 1623, 1485, 1307, 1131, 1094, 1001 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.05 (9H, s), 1.25 (9H, s), 4.48 (1H, s), 4.82 (1H, s), 7.11 (2H, t, J = 8.6 Hz), 8.03–8.07 (2H, m); ^{13}C NMR ($CDCl_3$) δ 25.4 (q), 25.9 (q), 36.4 (s), 37.4 (s), 98.4 (d), 98.5 (d), 115.7 (d), 115.9 (d), 130.7 (s), 130.8 (s), 157.8 (s), 165.5 (d, J = 254.3 Hz); Calcd for $C_{17}H_{24}FNO_3S$: C, 59.80; H, 7.08; N, 4.10%; Found: C, 59.92; H, 7.11; N, 4.12%.

2,6-Di-tert-butyl-4-(p-methoxyphenyl)-6H-1,3,5-oxathiazine S, S-dioxide (3d). Colorless crystals; mp 121–123 °C (decomp.); MS *m/z* 233 ($M^+ - t$BuCHOS − 2; 12%), 201 ($M^+ - MeOC_6H_4CN - t$BuCH − 2; 100%); IR (KBr) 2978, 1621, 1488, 1305, 1137, 1097 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.04 (9H, s), 1.12 (9H, s), 3.86 (3H,s), 4.09 (1H,s), 5.42 (1H,s), 6.94 (2H,d, J = 8.9 Hz), 7.58 (2H, d, J = 8.9 Hz); ^{13}C NMR ($CDCl_3$):δ 24.4 (q) 26.2 (q), 33.0 (s), 34.0 (s), 55.5 (q), 88.8 (d), 104.1 (d), 114.7 (d), 114.8 (s), 120.3 (s), 133.9 (d), 162.8 (s); Calcd for $C_{18}H_{27}NO_4S$: C, 61.16; H, 7.70; N, 3.96%; Found: C, 61.24; H, 7.74; N, 3.98%.

Lewis acid-induced thermal reaction of 6*H*-1,3,5-oxathiazine *S,S*-dioxides (3). A toluene solution (20 mL) of 6*H*-1,3,5-oxathiazine *S,S*-dioxide (**3**, 1.0 mmol) was treated with Lewis acid (silica gel or TsOH) (2.0 equiv) at refluxing temperature. The reaction mixture was quenched with aqueous Na_2SO_3 solution and was extracted with chloroform. The mixture was then subjected to the usual work-up. After removing the solvent in vacuo, the products **6** and **7** were separated by the silica gel chromatography.

Benzamide (6a). White powder, mp 127–132 °C; (Lit. [18], 130–131 °C).

4-Chloro-benzamide (6b). White powder, mp 176–180 °C (Lit. [18], 177–181 °C).

4-Fluoro-benzamide*, *(6c). White powder, mp 155–159 °C (Lit. [18], 154–158 °C).

4-Methoxy-benzamide (6d). collette White powder, mp 163–168 °C (Lit. [18], 164–167 °C).

Benzonitrile (7a). collette Clear liquid, (Lit. [19]); ^{1}H NMR ($CDCl_3$) δ 7.49 (2H, t), 7.62 (1H, t), 7.66 (2H, d).

4-Chloro-benzonitrile (7b). collette Pale yellow crystalline solid, mp 92–96 °C (Lit. [19], 92–94 °C).

4-Fluoro-benzonitrile (7c). Colorless solid, mp 32–36 °C (Lit. [20], 33–36 °C).

4-Methoxy-benzonitrile (7d). White crystalline powder, mp 55–62 °C (Lit. [19], 60–62 °C).

Preparation of 2,4,6-trisubstituted 6*H*-1,3,5-oxathiazine *S*-oxides (2) by *m*-CPBA oxidation of 6*H*-1,3,5-oxathiazines (1). A chloroform solution (20 mL) of 6*H*-1,3,5-oxathiazine (**1**, 1.0 mmol) was treated with *m*-CPBA (1.1 equiv) at 0 °C in the presence of $NaHCO_3$ (2 equiv). The reaction mixture was quenched with aqueous Na_2SO_3 solution and was extracted with chloroform. The mixture was then subjected to the usual work-up. After removing the solvent in vacuo, product **2** was found in almost quantitative yield as single epimers (**2a–d**).

2,6-Di-tert-butyl-4-phenyl-6H-1,3,5-oxathiazine S-oxide (2a). Pale yellow oil, (Lit. [14]); ^{1}H NMR ($CDCl_3$) δ 1.02 (9H, s), 1.22 (9H, s), 4.25 (1H, s), 4.99 (1H, s), 7.41–7.48 (3H, m), 7.91–7.94 (2H, m).

2,6-Di-tert-butyl-4-(p-chlorophenyl)-6H-1,3,5-oxathiazine S-oxide (2b). Pale yellow oil, (Lit. [14]); ^{1}H NMR ($CDCl_3$) δ 1.01 (9H, s), 1.18 (9H, s), 4.24 (1H, s), 4.98 (1H, s), 7.43 (2H, br d, J = 8.0 Hz), 7.87 (2H, br d, J = 8.0 Hz).

2,6-Di-tert-butyl-4-(p-fluorophenyl)-6H-1,3,5-oxathiazine S-oxide (2c). Pale yellow oil, (Lit. [14]); ^{1}H NMR ($CDCl_3$) δ 1.01 (9H, s), 1.19 (9H, s), 4.25 (1H, s), 4.98 (1H, s), 7.12 (2H, t, J = 8.7 Hz), 7.96 (2H, dd, J = 8.7, J = 5.4 Hz).

2,6-Di-tert-butyl-4-(p-methoxyphenyl)-6H-1,3,5-oxathiazine S-oxide (2d). Colorless prisms, mp 85–86 °C; (Lit. [14], 84–85 °C decomp.).

Thermal reaction of 6*H*-1,3,5-oxathiazine *S*-oxides (2). A benzene solution (20 mL) of 6*H*-1,3,5-oxathiazine *S*-oxide (**2**, 1.0 mmol) was heated at refluxing temperature for 4–6 h, and the reaction mixture was cooled to room temperature. After removing the solvent in vacuo, 5*H*-1,2,4-oxathiazoles **4a–d** were obtained as pure products in high yields.

5-tert-Butyl-3-phenyl-5H-1,2,4-oxathiazole (4a). Pale yellow oil, (Lit. [14]); ^{1}H NMR ($CDCl_3$) δ 1.08 (9H, s), 5.89 (1H, s), 7.40–7.46 (3H, m), 7.46–7.57 (2H, m).

5-tert-Butyl-3-(p-chlorophenyl)-5H-1,2,4-oxathiazole (4b). Pale yellow oil, (Lit. [14]); ^{1}H NMR ($CDCl_3$) δ 1.09 (9H, s), 5.87 (1H, s), 7.42 (2H, br d, J = 8.0 Hz), 7.51 (2H, br d, J = 8.0 Hz).

5-tert-Butyl-3-(p-fluorophenyl)-5H-1,2,4-oxathiazole (4c). Pale yellow oil, (Lit. [14]); ^{1}H NMR ($CDCl_3$) δ 1.09 (9H, s), 5.86 (1H, s), 7.12 (2H, t, J = 8.6 Hz), 7.58 (2H, dd, J = 8.6, J = 5.3 Hz).

5-tert-Butyl-3-(p-methoxyphenyl)-5H-1,2,4-oxathiazole (4d). Pale yellow oil, (Lit. [14]); ^{1}H NMR ($CDCl_3$) δ 1.06 (9H, s), 3.83 (3H, s), 5.85 (1H, s), 6.92(2H, d, J = 8.7 Hz), 7.52 (2H, d, J = 8.5 Hz).

Preparation of 5*H*-1,2,4-oxathiazole *S*-oxides 5 by *m*-CPBA oxidation of 5*H*-1,2,4-oxathiazoles 4. A chloroform solution (20 mL) of 5*H*-1,2,4-oxathiazoles (**4**, 1.0 mmol) was treated with *m*-CPBA (1.1 equiv) at 0 °C for 1 h in the presence of $NaHCO_3$ (2 equiv). The reaction mixture was quenched with aqueous Na_2SO_3 solution and was extracted with chloroform. The mixture was then subjected to the usual work-up. The solvent was evaporated in vacuo, and the crude product was subjected to chromatographic separation on silica gel. The products were obtained as inseparable epimeric mixture of 5*H*-1,2,4-oxathiazole *S*-oxides **5**.

5-tert-Butyl-3-phenyl-5H-1,2,4-oxathiazole S-oxide (5a). Pale yellow oil, (Lit. [14]); ^{1}H NMR ($CDCl_3$) major isomer δ 1.05 (9H, s), 6.62 (1H, s), 7.48–7.59 (3H, m), 8.04–8.05 (2H, m), minor isomer δ 1.12 (9H, s), 6.32 (1H, s), 7.48–7.59 (3H, m), 8.03–8.04 (2H, m).

5-tert-Butyl-3-(p-chlorophenyl)-5H-1,2,4-oxathiazole S-oxide (5b). Pale yellow oil, (Lit. [14]); ^{1}H NMR ($CDCl_3$) major isomer δ 1.07 (9H, s), 6.59 (1H, s), 7.51 (2H, d, J = 8.0 Hz), 7.97 (2H, d, J = 8.0 Hz), minor isomer δ 1.11 (9H, s), 6.30 (1H, s), 7.49 (2H, d, J = 8.0 Hz), 7.99 (2H, d, J = 8.0 Hz).

5-tert-Butyl-3-(p-fluorophenyl)-5H-1,2,4-oxathiazole S-oxide (5c). Pale yellow oil, (Lit. [14]); ^{1}H NMR ($CDCl_3$) major isomer δ 1.04 (9H, s), 6.59 (1H, s), 7.21 (2H, t, J = 8.8 Hz), 8.05–8.10 (2H, m), minor isomer δ 1.11 (9H, s), 6.31 (1H, s), 7.19 (2H, t, J = 8.6 Hz), 8.05–8.11 (2H, m).

5-tert-Butyl-3-(p-methoxyphenyl)-5H-1,2,4-oxathiazole S-oxide (5d). Pale yellow oil, (Lit. [14]); ^{1}H NMR ($CDCl_3$) major isomer δ 1.05 (9H, s), 3.88 (3H, s), 6.57 (1H, s), 7.01 (2H, d, J = 8.8 Hz), 7.98 (2H, d, J = 8.5 Hz), minor isomer δ 1.10 (9H, s), 3.84 (3H, s), 6.27 (1H, s), 6.99 (2H, d, J = 8.7 Hz), 8.01 (2H, d, J = 8.6 Hz).

Lewis acid-induced thermal reaction of 5*H*-1,2,4-oxathiazole *S*-oxides (5). A chloroform/toluene solution (20 mL) of *5H*-1,2,4-oxathiazole *S*-oxides (**5**, 1.0 mmol) was treated with Lewis acid (silica gel or TsOH) (2.0 equiv) at refluxing temperature. The reaction mixture was quenched with aqueous Na_2SO_3 solution and was extracted with chloroform. The mixture was then subjected to the usual work-up. After removing the solvent in vacuo, the products **6** and **7** were separated by the silica gel chromatography.

Benzamide (6a). White powder, mp 128–133 °C; (Lit. [18], 130–131 °C).

4-Chloro-benzamide (6b). White powder, mp 175–181 °C (Lit. [18], 177–181 °C).

4-Fluoro-benzamide (6c). White powder, mp 156–158 °C (Lit. [18], 154–158 °C).

4-Methoxy-benzamide (6d). White powder, mp 164–169 °C (Lit. [18], 164–167 °C).

Benzonitrile (7a). Clear liquid, (Lit. [19]); ^{1}H NMR ($CDCl_3$) δ 7.49 (2H, t), 7.62 (1H, t), 7.66 (2H, d);

4-Chloro-benzonitrile (7b). Pale yellow crystalline solid, mp 92–96 °C (Lit. [19], 92–94 °C).

4-Fluoro-benzonitrile (7c). Colorless solid, mp 32–36 °C (Lit. [20], 33–36 °C).

4-Methoxy-benzonitrile (7d). White crystalline powder, mp 55–62 °C (Lit. [19], 60–62 °C).

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