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Novel Conversion of 6*H*-1,3,5-Oxathiazine *S*-Oxides into 5-Membered Heterocyclic Compounds

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ABSTRACT: *5*H-*1,2,4-oxathiazoles were efficiently synthesized from 6*H-*1,3,5-oxathiazine* S-*oxides by thermal cycloreversion of the substrates and the products were effectively converted into 1,2,4-thiadiazoles.*
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INTRODUCTION

Heterocyclic compounds containing nitrogen, sulfur, and oxygen atoms have a great synthetic importance in the light of their potential biological profiles and multifunctional utilities. Various reactive intermediates containing nitrogen and sulfur functionalities in the same substructures have been developed as versatile building blocks for the synthesis of such heterocycles. Recently, a great deal of interest has been focused on the preparation and synthetic application of α,β-unsaturated thione *S*-oxides due to their heterocumulene-like structures and potential building blocks toward the synthesis of sulfur containing heterocyclic compounds. However, only a very limited studies concerning the heterodienes conjugated with a sulfine or sulfene framework have been realized due to the preparative difficulties of their precursors and lack of suitable trapping methods for these highly reactive species [1–15]. In the course of studies on highly-reactive heterodienes possessing chalcogen functionalities, several groups, including ours, have reported a convenient generation of 1,3-thiaza-1,3-butadienes **A** through thermal cycloreversion of 6*H*-1,3,5-oxathiazines **3** [16–19].

We envisaged that highly reactive 1,3-thiaza-1,3-butadiene *S*-oxides **B** would be generated through thermal cycloreversion of 6*H*-1,3,5-oxathiazine *S*-oxides **4** and their subsequent facile ring closure might give hitherto unknown 5*H*-1,2,4-oxathiazoles **5** as shown in Scheme 1. In accordance with our expectation, we successfully synthesized **5** via the most likely intermediate **B**. The synthetic applications of newly synthesized **5** were also explored. In this paper, we would like to report a full account of the new approach [20].

RESULTS AND DISCUSSION

6*H*-1,3,5-oxathiazines **3a–m** were prepared as single stereoisomers by treating an alkanethioamide

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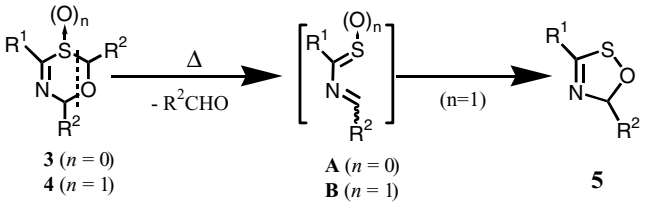


SCHEME 1

or an arenethioamide with an aliphatic aldehyde and $BF_3{\cdot}OEt_2$ according to the reported procedures [19–21]. The physical data of the compounds **3a–m** were fully consistent with their assigned structures. The relative stereochemistry of these products was confirmed to be *cis*-configuration in all cases by NOE measurements [22]. All results for the preparation of **3a–m** are shown in Table 1.

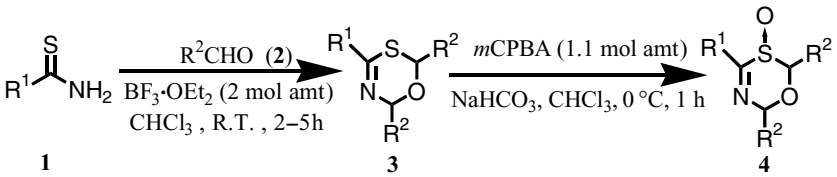
When a $CHCl_3$ solution of **3a–g** was treated with *m*CPBA (1.1 mol amt) at 0°C for 1 h, the corresponding *S*-oxides **4a–g** were obtained as single epimers in quantitative yields. The stereoselective formation of compounds **4a–g** might be due to the presence of a bulky substituent such as *t*-butyl or isopropyl group at the C-2 position of **3a–g**. The treatment of **3h–k** bearing a methyl or *n*-butyl group at the C-2 and C-6 positions with *m*CPBA (1.1 mol amt) afforded inseparable 3:1 epimeric mixtures of unstable compounds ascribed to **4h–k** besides recovered substrates **3h–k** (ca. 25%). In contrast, *m*CPBA oxidation of **3l** and **3m** afforded complex mixtures. All results concerning *m*CPBA oxidation of **3a–m** are shown in Table 1.

The complete relative stereochemistry of the S—O bond and the substituents at the C-2 and C-6 positions of **4** was determined to be equatorially-oriented by using X-ray crystallographic analysis of **4d**, and the ORTEP drawing is shown in Fig. 1.

Heating of a $CHCl_3$ or a benzene solution of *S*-oxides **4a–f** at refluxing temperature for several hours afforded 5*H*-1,2,4-oxathiazoles **5a–f** in high yields. The purification of **5a–f** was carried out by evacuation of volatile aldehydes at room temperature.

When a $CDCl_3$ solution of **4a** was kept standing in an NMR tube at 25 °C, a gradual increase in the intensities of the ^{1}H NMR and ^{13}C NMR signals of **5a** and pivalaldehyde was observed along with gradual decrease of the signals of **4a**. After standing the resulting solution for 300 h, a 1:1 mixture of **5a** and pivalaldehyde along with a small amount of 3,5-diphenyl-1,2,4-thiadiazoles **6a** was observed. This result might suggest that thermal cycloreversion of **4a** would generate 1,3-thiaza-1,3-butadiene *S*-oxide **B**, which subsequently causes facile ring closure to give

TABLE 1 Preparation of 6*H*-1,3,5-oxathiazines **3** and 6*H*-1,3,5-oxathiazine *S*-Oxides **4**



			Yield (%)	
Entry	R^1	R^2	**3**[a]	**4** *(major:minor)*
1	C_6H_5	*t*-C_4H_9	43 (**3a**)	96[a] (**4a**, 100:0)
2	*p*-ClC_6H_4	*t*-C_4H_9	32 (**3b**)	98[a] (**4b**, 100:0)
3	*p*-FC_6H_4	*t*-C_4H_9	25 (**3c**)	98[a] (**4c**, 100:0)
4	*p*-$CH_3OC_6H_4$	*t*-C_4H_9	45 (**3d**)	99[a] (**4d**, 100:0)
5	1-Naphthyl	*t*-C_4H_9	44 (**3e**)	97[a] (**4e**, 100:0)
6	C_6H_5	*i*-C_3H_7	21 (**3f**)	95[a] (**4f**, 100:0)
7	CH_3	*t*-C_4H_9	38 (**3g**)	97[a] (**4g**, 100:0)
8	C_6H_5	CH_3	95 (**3h**)	74[b] (**4h**, 3:1)[c]
9	*p*-ClC_6H_4	CH_3	38 (**3i**)	76[b] (**4i**, 3:1)[c]
10	*p*-FC_6H_4	CH_3	91 (**3j**)	75[b] (**4j**, 3:1)[c]
11	C_6H_5	*n*-C_4H_9	74 (**3k**)	73[b] (**4k**, 3:1)[c]
12	*t*-C_4H_9	*t*-C_4H_9	15 (**3l**)	Complex mixture
13	CH_3	CH_3	76 (**3m**)	Complex mixture

[a]Isolated yields.
[b]Based on the integration of ^{1}H NMR.
[c]Determined by the integration of the ^{1}H NMR spectra.

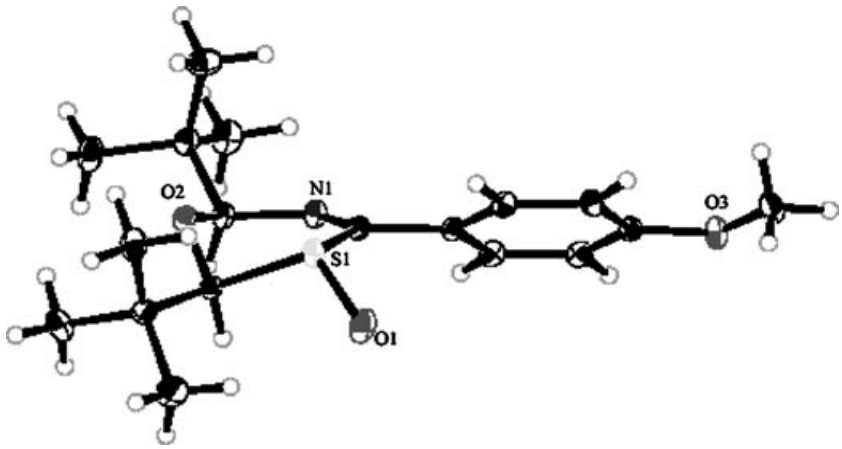


FIGURE 1 ORTEP drawing of **4d**. Selected bond lengths (Å), bond angles (°), and torsion angles (°): S1-O1 = 1.489(2); S1-C3 = 1.863(2); N1-C3 = 1.264(3); S1-C1 = 1.849(2); O2-C2 = 1.432(2); O1-S1-C1 = 109.5(10); S1-C1-C10 = 114.0(1); O2-C1-C10 = 111.2(2); O2-C2-C14 = 107.8(2); S1-C1-O2-C2 = 82.9(2); O1-S1-C1-C10 = 76.1(2).

5a. Further standing of the resulting mixture for an additional 500 h led to a 1:4 mixture of **6a** and pivalaldehyde along with precipitation of elemental sulfur.

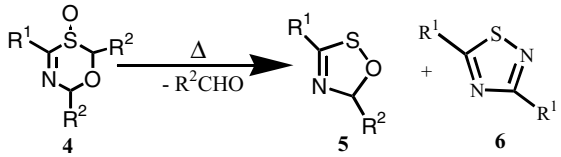
Thermolysis of **4g** in benzene at refluxing temperature for 4 h only gave a complex mixture. On the other hand, thermal reaction of the crude mixture of **4h–k** under similar conditions afforded inseparable products involving **5h–k**. In fact, the mixtures were converted into the corresponding 1,2,4-thiadiazoles **6** through the contact with silica gel. When a $CDCl_3$ solution of the isomeric mixture of **4h** (major:minor = 3:1) was kept standing in an NMR tube at room temperature for about a month, characteristic new signals at $\delta = 1.45$ ppm (d) and 6.30 ppm (q), most likely assigned to the methyl and methine protons of **5h**, respectively, were observed along with the early disappearance of the minor isomer of **4h** in the solution. This result suggests that the minor isomer of **4h** is more reactive toward thermal cycloreversion.

The physical data, including MS, IR, ^{1}H NMR, and ^{13}C NMR spectra, were fully consistent with the structures of 3-aryl-5-alkyl-5*H*-1,2,4-oxathiazoles **5a–f**. The oily compounds **5a–f** were labile toward the storage, so little deviation in their elemental analysis data to those of calculated ones was observed. All results of the thermal reaction of **4** are summarized in Table 2.

The preparation of stable derivatives of **5** was attempted. The oxidation of **5a–f** by *m*CPBA at 0°C afforded 3:1 oily inseparable epimers of **7a–f**. In the case of *m*CPBA oxidation of **5d**, nitrile **8d** was afforded as a minor product along with the epimeric mixture of the expected *S*-oxides **7d**. The formation of **8d** suggested that the push-pull type substituent effect of the electron-donating substituent, *p*-methoxyphenyl group, might accelerate the C—S bond cleavage. However, the stereoselective oxidation of **5** was not successful even when the oxidation was carried out at −78°C. The products **7**, except **7f**, were relatively stable toward the storage at room temperature and in contact with silica gel. The physical data, including MS, IR, ^{1}H NMR, and ^{13}C NMR spectra, as well as elemental analysis data were fully consistent with the structures of novel 3-aryl-5-alkyl-5*H*-1,2,4-oxathiazole *S*-oxides **7a–f**. Furthermore, these results unequivocally confirm the 5*H*-1,2,4-oxathiazole ring system in compound **5**. The results of the oxidation of **5** are summarized in Table 3.

Heating of an ethanolic solution of **4a** at refluxing temperature for 26 h gave thioamide **9a** [19] in 12% yield along with **6a** (35%) and small amount of unidentified products, and in this case, deoxygenated product **3a** was not found at all in crude reaction mixture. On the other hand, heating of an ethanolic solution of **5a** did not afford thioamide **9a**, instead partial conversion of **5a** into **6a** was found. This result indicates that **9a** is formed through the pathway involving the formation of heterodiene **B** followed by addition of ethanol to **B** and the subsequent deoxygenation of the resulting thioamide *S*-oxide **C** as shown in Scheme 2. Metzner reported that sulfine, very similar to the intermediate **C**, was deoxygenated through a plausible intermediate oxathiirane by electrocyclization and the subsequent oxygen atom was extruded under thermal condition [23]. We reported that when a toluene solution of **3** was heated in refluxing temperature in the presence of ethanol,

TABLE 2 Thermal Reaction of 6*H*-1,3,5-oxathiazine *S*-Oxides **4**



4 5 6

	Substrate						*Yield (%)*		
Entry	R^1	R^2	**4**	*Solvent*	*Temp (°C)*	*Time (h)*	**5**[a]	**6**	R^2CHO
1	C_6H_5	*t*-C_4H_9	**4a**	C_6H_6	Reflux	6	92 **(5a)**	0	–[b]
2	C_6H_5	*t*-C_4H_9	**4a**	$CDCl_3$	25	300	85[c] **(5a)**	15[c]	55[c]
3	C_6H_5	*t*-C_4H_9	**4a**	$CDCl_3$	25	800	0 **(5a)**	Quant	Quant[c]
4	*p*-ClC_6H_4	*t*-C_4H_9	**4b**	C_6H_6	Reflux	6	93 **(5b)**	0	–[b]
5	*p*-FC_6H_4	*t*-C_4H_9	**4c**	C_6H_6	Reflux	5	91 **(5c)**	0	–[b]
6	*p*-$CH_3OC_6H_4$	*t*-C_4H_9	**4d**	C_6H_6	Reflux	4	96 **(5d)**	0	–[b]
7	1-naphthyl	*t*-C_4H_9	**4e**	C_6H_6	Reflux	4	91 **(5e)**	0	–[b]
8	C_6H_5	*i*-C_3H_7	**4f**	C_6H_6	Reflux	4	89 **(5f)**	0	–[b]
9	CH_3	*t*-C_4H_9	**4g**	C_6H_6	Reflux	4	Complex mixture		
10	C_6H_5	CH_3	**4h**	C_6H_6	Reflux	4	–[d]	–[e]	–[b]
11	*p*-ClC_6H_4	CH_3	**4i**	C_6H_6	Reflux	4	–[d]	–[e]	–[b]
12	*p*-FC_6H_4	CH_3	**4j**	C_6H_6	Reflux	4	–[d]	–[e]	–[b]
13	C_6H_5	*n*-C_4H_9	**4k**	C_6H_6	Reflux	5	–[d]	–[e]	–[b]

[a]Isolated yields.
[b]Aldehydes were assumed to get away during the heating.
[c]Yields based on the integration of ^{1}H NMR spectrum of the reaction mixture.
[d]Compound **5** was not isolated from the thermal reaction products of the epimeric mixtures of **4**.
[e]Observed in the ^{1}H NMR spectrum of crude product of the thermal reaction of **4**.

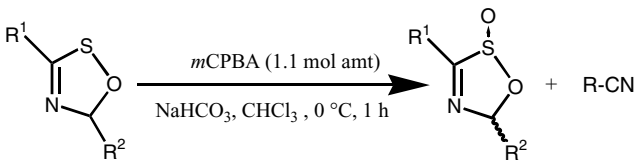
the 1,4-adduct **9** of heterodiene **A** was obtained in excellent yield [19]. In contrast, heating of the compound **4** afforded **5**, but did not give deoxygenated product **3**. These results exclude out the possibility of the involvement of heterodiene **A** in the formation of compound **9**. However, attempts for trapping of **B** using 2,3-dimethyl-1,3-butadiene, acetylenes, or allyltrimethylsilane were unsuccessful.

When a $CDCl_3$ solution of **5a** was heated at 100°C for 12 h in a sealed NMR tube, a 1:1 mixture of nitrile **8a** and pivalaldehyde along with elemental sulfur was formed. Treatment of a $CHCl_3$ solution of **5b** with Ph_3P (1.1 mol amt) at room temperature for 2 h afforded nitrile **8b** (89%) and $Ph_3P{=}S$ (86%) exclusively. Reaction of **5b** with benzylamine (1.2 mol amt) in $CHCl_3$ at room temperature for 12 h also afforded **8b** (93%). It is assumed that thiophilic attack of Ph_3P or benzylamine onto the sulfur atom of **5a** causes S–O bond fission to accelarate retro [2+2+1]-type cycloreversion.

It was found that 1,2,4-thiadiazoles **6** were efficiently obtained through the contact of **5** with silica gel as shown in Table 4.

Treating a benzene solution of **5a** with *p*-toluenesulfonic acid (1.1 mol amt) also gave a similar result. An independent ^{1}H NMR monitoring experiment for **5a** at 25°C in $CDCl_3$ also showed that the intensity of the signals for **5a** was gradually decreased and the signals ascribed to **6a** were increased along with those of pivalaldehyde. After 20 days, a mixture of **6a** and pivalaldehyde in 1:2 molar ratio was

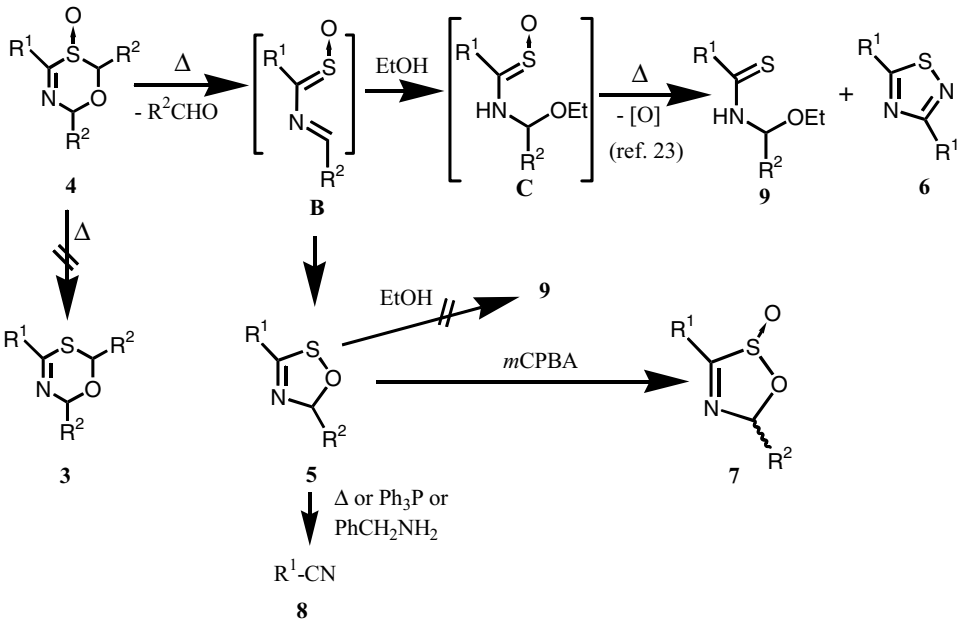
TABLE 3 Oxidation of 5*H*-1,2,4-oxathiazoles **5** by *m*CPBA



5 7 8

	Substrate			*Yield (%)*[a]	
Entry	R^1	R^2	**5**	**7** *(major:minor)*[b]	**8**
1	C_6H_5	*t*-C_4H_9	**5a**	88 (3:1)	0
2	*p*-ClC_6H_4	*t*-C_4H_9	**5b**	91 (3:1)	0
3	*p*-FC_6H_4	*t*-C_4H_9	**5c**	89 (3:1)	0
4	*p*-$MeOC_6H_4$	*t*-C_4H_9	**5d**	72 (3:1)	21
5	1-Naphthyl	*t*-C_4H_9	**5e**	87 (3:1)	0
6	C_6H_5	*i*-C_3H_7	**5f**	56 (3:1)	0

[a]Isolated yields.
[b]Ratios were determined by integration of the ^{1}H NMR spectra.

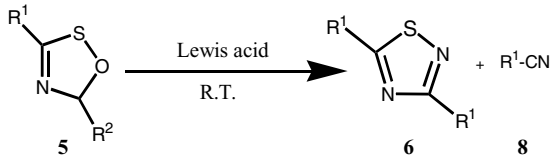


SCHEME 2 Plausible formation pathway of **5–9**.

afforded along with precipitated elemental sulfur. Moreover, heating of a $CHCl_3$ solution of **5a** at refluxing temperature for overnight gave a trace amount of **6a** along with the recovery of **5a**. It was thought that prolonged standing of $CDCl_3$ or $CHCl_3$ generates DCl or HCl, respectively, which might accelerate the ring cleavage of **5** and then subsequently lead to **6**.

When **4a** was directly treated with a Lewis acid, benzonitrile (**9a**) was mainly obtained along with small amounts of **6a**, 2,4,6-triphenyl-1,3,5-triazine

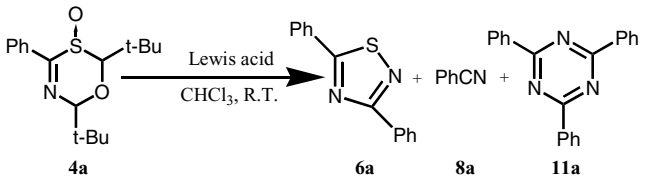
TABLE 4 Reaction of 5*H*-1,2,4-oxathiazoles **5** with Lewis Acids



	Substrates						*Yield (%)*[a]		
Entry	*R^1*	*R^2*	**5**	*Lewis Acid (Mol Amt)*	*Solvent*	*Time (h)*	**6**	**8**	*Recovery (%)*
1	C_6H_5	*t*-C_4H_9	**5a**	Silica gel (excess)	C_6H_6	1	82 **(6a)**	0	0
2	C_6H_5	*t*-C_4H_9	**5a**	*p*-TsOH(2.0)	C_6H_6	24	Quant **(6a)**	0	0
3	C_6H_5	*t*-C_4H_9	**5a**	DCl[b]	$CDCl_3$	800	Quant **(6a)**[c]	0	0
4	*p*-ClC_6H_4	*t*-C_4H_9	**5b**	Silica gel (excess)	C_6H_6	1	54 **(6b)**	0	21
5	*p*-FC_6H_4	*t*-C_4H_9	**5c**	Silica gel (excess)	C_6H_6	1	60 **(6c)**	0	20
6	*p*-$CH_3OC_6H_4$	*t*-C_4H_9	**5d**	Silica gel (excess)	C_6H_6	1	57 **(6d)**	31 **(8d)**	0
7	1-Naphthyl	*t*-C_4H_9	**5e**	Silica gel (excess)	C_6H_6	1	76 **(6e)**	0	0
8	C_6H_5	*i*-C_3H_7	**5f**	Silica gel (excess)	C_6H_6	1	79 **(6a)**	0	0
9	C_6H_5	CH_3	[d]	Silica gel (excess)	C_6H_6	1	50 **(6a)**[c]	0	0
10	*p*-ClC_6H_4	CH_3	[d]	Silica gel (excess)	C_6H_6	1	51 **(6b)**[c]	0	0
11	*p*-FC_6H_4	CH_3	[d]	Silica gel (excess)	C_6H_6	1	53 **(6c)**[c]	0	0
12	C_6H_5	*n*-C_4H_9	[d]	Silica gel (excess)	C_6H_6	1	56 **(6a)**[c]	0	0

[a]Isolated yields.
[b]It was assumed that DCl was generated through decomposition of $CDCl_3$.
[c]Estimated yield was based on the relative integrationof the ^1H NMR signals.
[d]The epimeric mixture of **4** was heated, and then the resulting mixture was taken in contact with silica gel.
[e]The yields were based on the starting **3**.

TABLE 5 Reaction of 6*H*-1,3,5-oxathiazine *S*-Oxide **4a** with Lewis Acids



			Yield (%)[a]		
Entry	*Lewis Acid (Mol Amt)*	*Time (h)*	**6a**	**8a**	**11a**
1	*p*-TsOH (1.0)	3	14	52	8
2	$BF_3{\cdot}OEt_2$ (1.0)	2	17	46	12
3	SiO_2 (excess)	2	28	39	6

[a]Isolated yields.

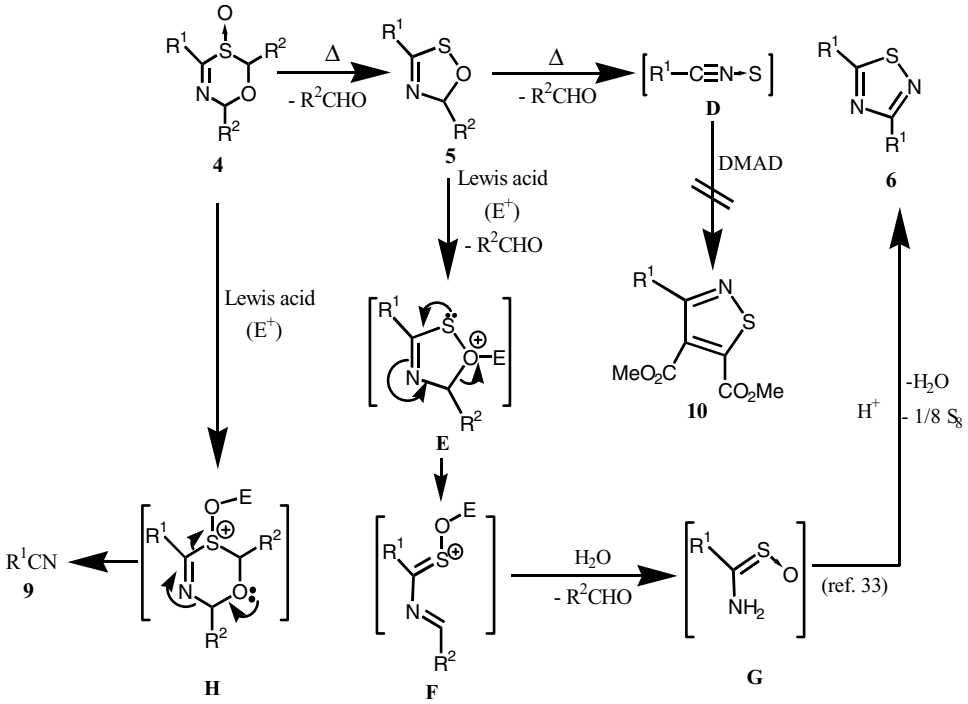
11a, and some unidentified compounds as shown in Table 5.

Several authors reported the formation of 1,2,4-thiadiazoles **6** through the intermediary nitrile sulfides **D** [24–29]. When a $CHCl_3$ solution of **4a** or **5a** was heated in the presence of DMAD, the possible cycloadduct **10** was not found at all in the crude reaction products. However, we could not fully exclude out the pathway involving **D** in the formation of **6** at this time. On the other hand, another alternative pathway for the formation of 1,2,4-thiadiazoles **6** through oxidative dimerization of primary thioamides are widely recognized [30–35].

With the above precedent in hand and taking our findings into account, now we would like to propose a plausible pathway for the conversion of **5** into **6** through acid-induced hydrolytic fragmentation of **5** as shown in Scheme 3. Lewis acid might coordinate with oxygen atom of **5** to form **F** *via* intermediate **E**. The subsequent hydrolysis of **F** might lead to intermediacy, thioamide *S*-oxide **G**. Our previous findings showed that when thioamide *S*-oxide was treated with electrophilic reagents or Lewis acids, the corresponding 3,5-disubstituted 1,2,4-thiadiazole was efficiently afforded [33]. In the present case, it was assumed that the resulting thioamide *S*-oxides **G** might also cause self-condensation by contact with silica gel or *p*-toluenesulfonic acid to give **6**. On the other hand, nitrile **9** would afford by acid-induced ring fission of **4** *via* intermediate **H**.

CONCLUSION

We have synthesized novel 5*H*-1,2,4-oxathiazoles **5** ring system through thermal cycloreversion of 6*H*-1,3,5-oxathiazines *S*-oxides **4** and the synthetic application of **5** into five-membered heterocyclic compounds containing nitrogen, oxygen, and sulfur atoms including 3,5-disubstituted 1,2,4-thiadiazoles **6** was also explored.



SCHEME 3 Plausible mechanism for the formation of **6**, and **9** (from **4**).

EXPERIMENTAL

General

Melting points were measured in open capillary tubes with a Buchi 535 micro-melting point apparatus and are uncorrected. ^{1}H NMR spectra were determined at 400 MHz (Bruker AC-400P spectrometer), and ^{13}C NMR spectra were determined at 100 MHz (Bruker AC-400P spectrometer). Chemical shifts are expressed in parts per million (δ units) downfield from tetramethylsilane (TMS) used as an internal reference. Mass spectra were recorded on a Hitachi M-2000 mass spectrometer 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. Elemental analyses were performed using a Yanagimoto CHN recorder MT-5. 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 6H-1,3,5-oxathiazines (**3**)*

A 20 ml chloroform solution of alkanethioamide or an arenethioamide **1** (10.0 mmol) was treated with 2,4,6-trimethyl-1,3,5-trioxane (paraldehyde **2a**, 1.04 g, 8.00 mmol), pivalaldehyde (**2b**, 2.06 g, 24.0 mmol), pentanal (**2c**, 2.06 g, 24.0 mmol), or isobutyraldehyde (**2d**, 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 (**3**) 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 (**3a**).* Colorless plates, mp 95.1–95.9°C (Lit. [19], 95.4–96.0°C).

*2,6-Di-tert-butyl-4-(p-chlorophenyl)-6H-1,3,5-oxathiazine (**3b**).* Colorless crystals, mp 95.5–96.1°C (decomp.) (Lit. [19], 95.4–96.0°C decomp.).

*2,6-Di-tert-butyl-4-(p-fluorophenyl)-6H-1,3,5-oxathiazine (**3c**).* Colorless plates, mp 55.5–56.5°C (decomp.); MS *m/z* (%) 309 (M^+; 2), 252 ($M^+ - t$-C_4H_9; 42), 223 ($M^+ - t$-C_4H_9CHO; 5), 139 (*p*-FC_6H_4CS; 36), 103 (bp); IR (KBr) 2954, 1610, 1506, 1478, 1362, 1237, 1068, 837 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.05 (9H, s), 1.06 (9H, s), 4.82 (1H, s), 4.97 (1H, s), 7.06 (2H, t, $J_{H\text{-}F} = J_{H\text{-}H} = 8.6$ Hz), 7.85 (2H, dd, $J_{H\text{-}H} = 8.6$ Hz, $J_{H\text{-}F} = 5.3$ Hz); ^{13}C NMR ($CDCl_3$) δ 25.1 (q), 25.3 (q), 36.1 (s), 36.9 (s), 88.8 (s), 96.9 (br s), 115.2 (dd, $J_{C\text{-}F} = 21.6$ Hz), 128.3 (dd, $J_{C\text{-}F} = 8.6$ Hz), 135.4 (d, $J_{C\text{-}F} = 2.5$ Hz), 156.4 (s), 164.2 (d, $J_{C\text{-}F} = 248.0$ Hz). Found: C, 65.90; H, 7.80; N, 4.55%. Calcd for $C_{17}H_{24}FNOS$: C, 65.98; H, 7.82; N, 4.53%.

*2,6-Di-tert-butyl-4-(p-methoxyphenyl)-6H-1,3,5-oxathiazine (**3d**).* Colorless needles, mp 101°C; MS *m/z* (%) 321 (M^+; 2), 264 ($M^+ - C_4H_9$; bp); IR (neat) 2914, 2353, 1683, 1538, 1071, 562 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.05 (9H, s), 1.06 (9H, s), 3.82 (3H,s), 4.82 (1H, s), 4.94 (1H, s), 6.89 (2H, d, $J = 9.0$ Hz), 7.81 (2H, d, $J = 8.8$ Hz); ^{13}C NMR ($CDCl_3$): δ 25.1 (q) 25.3 (q), 36.0 (s), 36.9 (s), 55.36 (q), 88.6 (s), 96.8 (br s), 113.5 (d), 127.8 (d), 132.0 (s), 156.5 (s), 161.6 (s); Found: C, 67.21; H, 8.51; N, 4.39%. Calcd for $C_{18}H_{27}NO_2S$: C, 67.25; H, 8.47; N, 4.36%.

*2,6-Di-tert-butyl-4-naphthalen-1-yl-6H-1,3,5-oxathiazine (**3e**).* Colorless crystals; mp 54–56°C (decomp.); MS *m/z* (%) 341 (M^+; 7), 284 ($M^+ - C_4H_9$; 50), 254 (bp); IR (neat): 2908, 1619, 1460, 1362, 1097, 1063, 999, 799 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.05 (9H, s), 1.11 (9H, s), 4.77 (1H, s), 5.15 (1H, s), 7.42–7.51 (3H, m), 7.63 (1H, d, $J = 7.1$ Hz), 7.82 (2H, dd, $J = 13.1$, 6.7 Hz), 8.40 (1H, d, $J = 8.2$ Hz); ^{13}C NMR ($CDCl_3$): δ 24.9 (q), 25.4 (q), 36.1 (s), 36.6 (s), 89.4 (br s), 97.3 (br s), 124.9 (s), 125.4 (d), 126.0 (s), 126.1 (d), 126.4 (d), 128.1 (d), 129.7 (d), 133.8 (s), 137.8 (s), 159.6 (s); Found: C, 74.23; H, 8.21; N, 4.07%. Calcd for $C_{21}H_{27}NOS$: C, 73.86; H, 7.97; N, 4.10%.

*2,6-Diisopropyl-4-phenyl-6H-1,3,5-oxathiazine (**3f**).* Pale yellow oil; MS *m/z* (%) 263 (M^+; 74), 191 (bp); IR (neat): 2967, 1615, 1470, 763 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.05 (6H, dd, $J = 6.2$, 6.1 Hz), 1.08 (6H, dd, $J = 6.3$, 6.2 Hz), 2.06 (1H, quint, $J = 6.5$ Hz), 2.16 (1H, quint, $J = 6.5$ Hz), 5.00 (1H, d, $J = 1.5$ Hz), 5.01 (1H, d, $J = 2.5$ Hz), 7.36–7.42 (3H, m), 7.82–7.84 (2H, m); ^{13}C NMR ($CDCl_3$): 17.2 (q), 17.4 (q), 17.6 (q), 17.7 (q), 33.9 (d), 34.2 (d), 85.3 (d), 94.2 (d), 126.3 (d), 128.2 (d), 130.7 (d), 139.0 (s), 157.5 (s); Found: C, 67.96; H, 7.97; N, 4.31%. Calcd for $C_{15}H_{21}NOS$: C, 68.40; H, 8.04; N, 4.32%.

*2,6-Di-tert-butyl-4-methyl-6H-1,3,5-oxathiazine (**3g**).* Colorless plates, mp 58.4–58.8 °C; MS *m/z*

(%) 229 (M^+; 1), 38 (bp); IR (KBr) 2958, 2868, 1642, 1478, 1460, 1204, 1091 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.97 (9H, s), 0.98 (9H, s), 2.14 (3H, s), 4.49 (1H, s), 4.87 (1H, s); ^{13}C NMR ($CDCl_3$) δ 24.9 (q), 25.1 (q), 29.0 (q), 35.8 (s), 36.2 (s), 88.4 (br s), 96.5 (d), 157.3 (s); Found: C, 62.48; H, 9.96; N, 6.06%. Calcd for $C_{12}H_{23}NOS$: C, 62.83; H, 10.11; N, 6.11%.

*2,6-Dimethyl-4-phenyl-6H-1,3,5-oxathiazine (***3h***).* Pale yellow oil, (Lit. [19]); MS *m/z* (%) 207 (M^+; 17), 165 (21), 39 (bp); IR (neat) 2985, 1614, 1447, 1373, 1323, 1231, 1161, 1114, 961, 766, 692, cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.60 (3H, d, $J = 6.1$ Hz), 1.61 (3H, d, $J = 6.2$ Hz), 5.28 (1H, q, $J = 6.2$ Hz), 5.35 (1H, q, $J = 6.1$ Hz), 7.35–7.43 (3H, m), 7.78–7.80 (2H, m); ^{13}C NMR ($CDCl_3$): 22.2 (q), 22.5 (q), 75.6 (s), 87.4 (d), 126.2 (d), 128.3 (d), 130.7 (d), 138.5 (s), 157.0 (s); Found: C, 63.45; H, 6.54; N, 6.37%. Calcd for $C_{11}H_{13}NOS$: C, 63.74; H, 6.32; N, 6.76%.

*4-(p-Chlorophenyl)-2,6-dimethyl-6H-1,3,5-oxathiazine (***3i***).* Colorless needles, mp 101.8–102.3°C (decomp.) (Lit. [19], 101.9–102.5°C (decomp.)).

*2,6-Dimethyl-4-(p-fluorophenyl)-6H-1,3,5-oxathiazine (***3j***).* Pale yellow plates; mp 47–48 °C (decomp.); MS *m/z* (%) 226 ($M^+ - 1$; 75), 185 ($M^+ - CH_3CHO$, 24), 139 (bp); IR (KBr) 2986, 1603, 1508, 1232, 1155, 962, 842 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.60 (3H, d, $J = 6.1$ Hz), 1.61 (3H, d, $J = 6.1$ Hz), 5.27 (1H, q, $J = 6.1$ Hz), 5.34 (1H, q, $J = 6.1$ Hz), 7.06 (2H, t, $J = 8.6$ Hz), 7.79 (2H, dd, $J = 8.6$, 5.4 Hz); ^{13}C NMR ($CDCl_3$) δ 22.2 (q), 22.4 (q), 75.6 (s), 87.3 (d), 115.2 (dd, $J_{C\text{-}F} = 21.7$ Hz), 128.2 (dd, $J_{C\text{-}F} = 8.7$ Hz), 134.6 (d, $J_{C\text{-}F} = 2.8$ Hz), 155.7 (s), 164.3 (d, $J_{C\text{-}F} = 249.9$ Hz); Found: C, 58.42; H, 5.29; N, 6.12%. Calcd for $C_{11}H_{12}FNOS$: C, 58.65; H, 5.37; N, 6.22%.

*2,6-Di-n-butyl-4-phenyl-6H-1,3,5-oxathiazine (***3k***).* Pale yellow oil; MS *m/z* (%) 292 ($M^+ + 1$; 1), 162 (bp); IR (neat): 2960, 1687, 1615, 1448, 1213, 1080, 1006, 766, 691 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.96 (3H, t, $J = 6.1$ Hz), 0.99 (3H, t, $J = 6.1$ Hz), 1.45–1.65 (4H, m), 1.68–1.81 (4H, m), 1.82–1.98 (4H, m), 5.18 (1H, t, $J = 3.5$ Hz), 5.20 (1H, t, $J = 4.0$ Hz), 7.35–7.39 (3H, m), 7.79–7.81 (2H, m); ^{13}C NMR ($CDCl_3$): 13.6 (q), 13.9 (q), 17.8 (t), 38.2 (t), 38.4 (t), 79.5 (d), 90.2 (d), 126.1 (d), 128.1 (d), 130.6 (d), 138.7 (s), 156.8 (s); Found: C, 69.62; H, 8.49; N, 5.02%. Calcd for $C_{17}H_{25}NOS$: C, 70.06; H, 8.65; N, 4.81%.

*2,4,6-Tri-tert-butyl-6H-1,3,5-oxathiazine (***3l***).* Colorless plates, mp 59.0–60.0°C; MS *m/z* (%) 271 (M^+; 9), 214 ($M^+ - t\text{-}C_4H_9$; 66), 188 ($M^+ - t\text{-}C_4H_9CN$; 99), 130 (bp); IR (KBr) 2964, 1625, 1479, 1361, 1068 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (9H, s), 0.98 (9H, s), 1.17 (9H, s), 4.57 (1H, s), 4.76 (1H, s); ^{13}C NMR ($CDCl_3$) δ 25.1 (q), 28.3 (q), 30.8 (q), 30.9 (s), 36.5 (s), 42.5 (s), 87.8 (d), 96.1 (d), 136.5 (s). Found: C, 65.90; H, 10.71; N, 5.07%. Calcd for $C_{15}H_{29}NOS$: C, 66.37; H, 10.77; N, 5.16%.

*2,4,6-Trimethyl-6H-1,3,5-oxathiazine (***3m***).* Pale yellow oil, (Lit. [21]); MS *m/z* (%) 145 (M^+; 1); ^1H NMR ($CDCl_3$): δ 1.50 (3H, d, $J = 6.2$ Hz), 1.52 (3H, d, $J = 6.1$ Hz), 2.13 (3H, s), 5.04 (1H, m), 5.20 (1H, q, $J = 6.1$ Hz).

*Preparation of 2,4,6-Trisubstituted 6H-1,3,5-oxathiazine S-Oxides (***4***) by mCPBA Oxidation of 6H-1,3,5-oxathiazines (***3***)*

A chloroform solution (20 ml) of 6*H*-1,3,5-oxathiazine (**3**, 1.0 mmol) was treated with *m*CPBA (1.1 mol amt) at 0°C in the presence of $NaHCO_3$ (2 mol amt). The reaction mixture was quenched with aqueous Na_2SO_3 solution and was extracted with chloroform. The mixture was then subjected to the usual workup. After removing the solvent in vacuo, product **4** was found in almost quantitative yield as single epimers (**4a–g**), or diastereomeric mixtures (**4h–k**).

*2,6-Di-tert-butyl-4-phenyl-6H-1,3,5-oxathiazine S-Oxide (***4a***).* Pale yellow oil; MS *m/z* (%) 221 ($M^+ - t\text{-}C_4H_9CHO$; 15), 164 ($M^+ - t\text{-}C_4H_9CHO\text{-}t\text{-}C_4H_9$; bp); IR (neat) 2961, 2870, 1634, 1479, 1365, 1064, 769, 690, 638 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.01 (9H, s), 1.21 (9H, s), 4.25 (1H, s), 4.99 (1H, s), 7.41–7.47 (3H, m), 7.91–7.93 (2H, m); ^{13}C NMR ($CDCl_3$) δ 24.9 (q), 25.6 (q), 35.8 (s), 37.0 (s), 97.7 (d), 98.6 (d), 128.9 (d), 129.9 (d), 130.8 (d), 132.0 (s), 163.3 (s). Found: C, 66.17; H, 8.10; N, 4.64%. Calcd for $C_{17}H_{25}NO_2S$: C, 66.41; H, 8.20; N, 4.56%.

*2,6-Di-tert-butyl-4-(p-chlorophenyl)-6H-1,3,5-oxathiazine S-Oxide (***4b***).* Pale yellow oil; MS *m/z* (%) 255 ($M^+ - t\text{-}C_4H_9CHO$; 60), 169 ($M^+ - 2t\text{-}C_4H_9$); 38), 103 (bp); IR (neat) 2960, 2339, 1626, 1592, 1488, 1364, 1092, 1067, 832 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (9H, s), 1.19 (9H, s), 4.24 (1H, s), 4.98 (1H, s), 7.42 (2H, br d, $J = 8.0$ Hz), 7.87 (2H, br d, $J = 8.0$ Hz); ^{13}C NMR ($CDCl_3$) δ 25.0 (q), 25.7 (q), 35.9 (s), 37.1 (s), 97.9 (d), 98.9 (br s), 128.6 (d), 130.4 (d), 131.1 (s), 137.3 (s), 162.5 (s). Found: C, 59.21; H, 6.79; N,

3.95%. Calcd for $C_{17}H_{24}ClNO_2S$: C, 59.72; H, 7.08; N, 4.10%.

*2,6-Di-tert-butyl-4-(p-fluorophenyl)-6H-1,3,5-oxathiazine S-Oxide (***4c***).* Pale yellow oil; MS *m/z* (%) 239 ($M^+ - t$-C_4H_9CHO; 11), 182 ($M^+ - t$-C_4H_9CHO-t-C_4H_9; bp); IR (neat) 2977, 2358, 1633, 1600, 1506, 1365, 1234, 1160, 1066, 839 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (9H, s), 1.19 (9H, s), 4.24 (1H, s), 4.98 (1H, s), 7.12 (2H, t, $J = 8.7$ Hz), 7.95 (2H, dd, $J = 8.7$, $J = 5.4$ Hz); ^{13}C NMR ($CDCl_3$) δ 25.0 (q), 25.7 (q), 35.9 (s), 37.1 (s), 97.9 (d), 98.7 (s), 115.5 (dd, $J_{C\text{-}F} = 21.8$ Hz), 128.9 (d, $J_{C\text{-}F} = 2.5$ Hz), 131.3 (dd, $J_{C\text{-}F} = 8.7$ Hz), 162.2 (s), 164.2 (d, $J_{C\text{-}F} = 250.8$ Hz). Found: C, 62.46; H, 7.12; N, 4.28%. Calcd for $C_{17}H_{24}FNO_2S$: C, 62.74; H, 7.43; N, 4.30%.

*2,6-Di-tert-butyl-4-(p-methoxyphenyl)-6H-1,3,5-oxathiazine S-Oxide (***4d***).* Colorless prisms, mp 84–85°C; MS *m/z* (%) 251 ($M^+ - t$-C_4H_9CHO; 17), 165 ($M^+ - p$-$CH_3OC_6H_4CN$; 6), 134 (t-C_4H_9CHOSO; 66), 139 (bp); IR (KBr) 2960, 1604, 1510, 1259, 1175, 1066, 1034 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.00 (9H, s), 1.19 (9H, s), 3.83 (3H,s), 4.27 (1H,s), 4.96 (1H,s), 6.93 (2H,d, $J = 8.9$ Hz), 7.92 (2H, d, $J = 8.9$ Hz); ^{13}C NMR ($CDCl_3$): δ 25.0 (q) 25.6 (q), 35.9 (s), 37.0 (s), 55.3 (q), 97.8 (d), 98.5 (br s), 113.7 (d), 125.3 (s), 130.7 (d), 161.8 (s), 162.0 (s); Found: C, 63.60; H, 7.88; N, 4.19%. Calcd for $C_{18}H_{27}NO_3S$: C, 64.06; H, 8.06; N, 4.15%.

*2,6-Di-tert-butyl-4-naphthalen-1-yl-6H-1,3,5-oxathiazine S-Oxide (***4e***).* Pale yellow oil; MS *m/z* (%) 271 ($M^+ - t$-C_4H_9CHO; 2), 185 ($M^+ - 2$-t-C_4H_9CHO; 3), 153 ($C_{10}H_7CN$; bp); IR (neat): 2963, 1645, 1480, 1365, 1100, 1062, 774 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.06 (9H, s), 1.21 (9H, s), 4.28 (1H, s), 5.15 (1H, s), 7.51-7.53 (3H, m), 7.71 (1H, d, $J = 7.0$ Hz), 7.87 (1H, d, $J = 7.7$ Hz), 7.92 (1H, d, $J = 8.2$ Hz), 8.21 (1H, d, $J = 8.3$ Hz); ^{13}C NMR ($CDCl_3$): δ 25.1 (q), 25.6 (q), 36.0 (s), 36.9 (s), 97.9 (d), 99.5 (br s), 124.6 (d), 124.9 (d), 126.3 (s), 127.0 (d), 126.4 (d), 128.0 (d), 128.6 (d), 130.6 (d), 130.9 (d), 133.7 (s), 167.1 (s); Found: C, 74.23; H, 8.21; N, 4.07%. Calcd for $C_{21}H_{27}NOS$: C, 73.86; H, 7.97; N, 4.10%.

*2,6-Diisopropyl-4-phenyl-6H-1,3,5-oxathiazine S-Oxide (***4f***).* Pale yellow oil; MS *m/z* (%) 279 (M^+; 5), 207 ($M^+ - C_3H_7CHO$; 31), 104 (bp); IR (neat): 2970, 1629, 1471, 1035, 761 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.99 (6H, dd, $J = 6.8$, 6.8 Hz), 1.17 (6H, dd, $J = 6.8$, 6.8 Hz), 2.12 (1H, quint, $J = 3.5$ Hz), 2.51 (1H, quint, $J = 3.5$ Hz), 4.42 (1H, d, $J = 3.5$ Hz), 5.19 (1H, d, $J = 4.5$ Hz), 7.39–7.48 (3H, m), 7.92–7.94 (2H, m); ^{13}C NMR ($CDCl_3$): 16.2 (q), 16.6 (q), 17.2 (q), 18.2 (q), 29.4 (d), 33.8 (d), 94.9 (d), 95.7 (d), 127.7 (s), 128.2 (d), 128.8 (d), 131.0 (d), 163.3 (s); Found: C, 63.93; H, 7.41; N, 5.09%. Calcd for $C_{15}H_{21}NO_2S$: C, 64.48; H, 7.58; N, 5.01%.

*2,6-Di-tert-butyl-4-methyl-6H-1,3,5-oxathiazine S-Oxide (***4g***).* Pale yellow oil; MS *m/z* (%) 158 ($M^+ - t$-C_4H_9CHO; 5), 42 (bp); IR (neat) 2960, 1662, 1541, 1481, 1369, 1255, 1049 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.95 (9H, s), 1.14 (9H, s), 2.45(3H, d, $J = 2.5$, 2.4 Hz), 4.02(1 s); ^{13}C NMR ($CDCl_3$) δ 19.6 (q), 24.8 (q), 25.4 (q), 35.6 (s), 36.4 (s), 96.7 (d), 99.0 (d), 165.4 (s); Found: C, 58.93; H, 9.41; N, 5.68%. Calcd for $C_{12}H_{23}NO_2S$: C, 58.74; H, 9.45; N, 5.71%.

*Thermal Reaction of 6H-1,3,5-oxathiazine S-Oxides (***4***)*

A benzene solution (20 ml) of 6*H*-1,3,5-oxathiazine *S*-oxide (**4**, 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 **5a–g** were obtained as pure products in high yields.

*5-tert-Butyl-3-phenyl-5H-1,2,4-oxathiazole (***5a***).* Pale yellow oil; MS *m/z* (%) 221 (M^+; 18), 164 ($M^+ - t$-C_4H_9, bp), 57 (t-C_4H_9, 42); IR (neat) 2959, 1620, 1477, 1450, 1364, 1328, 1056, 969, 765, 714, 689 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09 (9H, s), 5.89 (1H, s), 7.40–7.45 (3H, m), 7.47–7.57 (2H, m); ^{13}C NMR ($CDCl_3$) δ 25.2 (q), 37.3 (s), 123.6 (d), 128.0 (d), 128.8 (d), 130.0 (s), 132.0 (d), 168.2 (s). Found: C, 63.97; H, 6.69; N, 6.16%. Calcd for $C_{12}H_{15}NOS$: C, 65.12; H, 6.83; N, 6.33%.

*5-tert-Butyl-3-(p-chlorophenyl)-5H-1,2,4-oxathiazole (***5b***).* Pale yellow oil; MS *m/z* (%) 255 (M^+; 22), 43 (bp); IR (neat) 2959, 2400, 1621, 1489, 1364, 1092, 971, 833 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (9H, s), 5.87 (1H, s), 7.42 (2H, br d, $J = 8.0$ Hz), 7.50 (2H, br d, $J = 8.0$ Hz); ^{13}C NMR ($CDCl_3$) δ 25.2 (q), 37.4 (s), 123.7 (d), 128.4 (s), 129.2 (d), 129.3 (d), 138.0 (s), 167.2 (s). Found: C, 55.25; H, 5.53; N, 5.27%. Calcd for $C_{12}H_{14}ClNOS$: C, 56.35; H, 5.52; N, 5.48%.

*5-tert-Butyl-3-(p-fluorophenyl)-5H-1,2,4-oxathiazole (***5c***).* Pale yellow oil; MS *m/z* (%) 239 (M^+; 4), 41 (bp); IR (neat) 2959, 1621, 1508, 1235, 1156, 1058, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (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); ^{13}C NMR ($CDCl_3$) δ 25.2 (q), 37.3 (s), 116.0 (dd, $J_{C\text{-}F} = 22.3$ Hz), 123.6 (d), 126.2 (d, $J_{C\text{-}F} = 2.5$ Hz), 130.2 (dd, $J_{C\text{-}F} = 7.7$ Hz), 164.7 (d,

$J_{C\text{-}F}$ = 251.4 Hz), 167.0 (s). Found: C, 58.86; H, 5.75; N, 5.48%. Calcd for $C_{12}H_{15}FNOS$: C, 60.23; H, 5.90; N, 5.85%.

*5-tert-Butyl-3-(p-methoxyphenyl)-5H-1,2,4-oxathiazole (***5d***).* Pale yellow oil; MS *m/z* (%) 251 (M^+; 16), 194 ($M^+ - C_4H_9$, 72), 41 (bp); IR (neat) 2960, 2226, 1608, 1510, 1261, 1173, 1060, 1032, 970, 835 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (9H, s), 3.83 (3H,s), 5.85 (1H, s), 6.91(2H, d, J = 8.7 Hz), 7.52 (2H, d, J = 8.5 Hz)**;** ^{13}C NMR ($CDCl_3$) δ 25.2 (q), 37.3 (s), 55.3 (q), 113.9 (d), 122.6 (s), 123.4 (d), 129.7 (d), 162.4 (s), 167.4 (s). Found: C, 61.57; H, 6.55; N, 5.42%. Calcd for $C_{13}H_{17}NO_2S$: C, 62.12; H, 6.82; N, 5.57%.

*5-tert-Butyl-3-naphthalen-1-yl-5H-1,2,4-oxathiazole (***5e***).* Pale yellow oil; MS *m/z* (%) 271 ($M^+ - t$-C_4H_9CHO; 2), 239 ($M^+ - S$; 2); 185 ($M^+ - t$-C_4H_9CHO; 89), 153 ($C_{10}H_7CN$; bp); IR (neat): 2964, 2222, 1512, 1213, 1142, 802, 773 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.18(9H, s), 6.06 (1H, s), 7.45–7.62 (3H, m), 7.95 (1H, d, J = 8.3 Hz), 8.06 (1H, d, J = 8.3 Hz), 8.23 (1H, d, J = 8.3 Hz), 8.93 (1H, d, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$): δ 25.4 (q), 37.4 (s), 110.20 (d), 124.2 (s), 124.7 (d), 124.9 (d), 126.6 (d), 127.5 (d), 127.8 (s), 128.5 (d), 128.6 (d), 132.2 (d), 132.6 (s), 168.0 (s). Found: C, 69.77; H, 6.24; N, 5.11%. Calcd for $C_{16}H_{17}NOS$: C, 70.81; H, 6.31; N, 5.16%.

*5-Isopropyl-3-phenyl-5H-1,2,4-oxathiazole (***5f***).* Pale yellow oil; MS *m/z* (%) 207 (M^+; 19), 164 ($M^+ - C_3H_7$; bp); IR (neat): 2966, 2230, 1618, 14761328, 1119, 1027, 763, 690 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.08 (6H, dd, J = 6.8, 6.8 Hz), 2.26 (1H, quint, J = 4.9 Hz), 6.02 (1H, d, J = 4.8 Hz), 7.41–7.51 (3H, m), 7.57–7.59 (2H, m); ^{13}C NMR ($CDCl_3$): 17.3 (q), 17.6 (q), 33.5 (d), 120.5 (d), 127.4 (s), 128.0 (d), 128.8 (d), 132.0 (d), 168.4 (s**)**. Found: C, 62.46; H, 6.18; N, 6.33%. Calcd for $C_{11}H_{13}NOS$: C, 63.73; H, 6.32; N, 6.76%.

Conversion of 5H-1,2,4-oxathiazoles **5** *into 3,5-Disubstituted 1,2,4-Thiadiazoles* **6** *by the Treatment of Silica Gel/Lewis Acid*

A chloroform solution of 5*H*-1,2,4-oxathiazoles (**5**, 1.0 mmol) was transferred onto a column, packed with silica gel. The crude product was allowed to stand for an hour. Then separation was performed by using hexane as eluent. The products **6** were obtained as solid except **6e**. The solid products **6** were purified by recrystallization from hexane.

*3,5-Diphenyl-1,2,4-thiadiazole (***6a***).* Colorless needles, mp 88.5–89.7°C (Lit. [33], 91.0°C).

*3,5-Bis-(p-chlorophenyl)-1,2,4-thiadiazole (***6b***).* Colorless needles, mp 159–161°C (Lit. [33], 161–162°C).

*3,5-Bis-(p-fluorophenyl)-1,2,4-thiadiazole (***6c***).* Colorless needles, mp 185–186°C; MS *m/z* (%) 273 ($M^+ - 1$; 98), 88 (bp) 32 (S, 58); IR (KBr) 1598, 1518, 1478, 1411, 1316, 1237, 1158, 1098, 806, 743 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15–7.25 (6H, m), 8.03–8.06 (2H, m), 8.35–8.39 (2H, m); ^{13}C NMR ($CDCl_3$) δ 115.8 (dd, $J_{C\text{-}F}$ = 21.1 Hz), 116.6 (dd, $J_{C\text{-}F}$ = 21.7 Hz), 127.0 (d, $J_{C\text{-}F}$ = 2.5 Hz), 129.1 (d, $J_{C\text{-}F}$ = 2.5 Hz), 129.7 (dd, $J_{C\text{-}F}$ = 8.8 Hz), 130.5 (dd, $J_{C\text{-}F}$ = 8.8 Hz), 164.2 (d, $J_{C\text{-}F}$ = 248 Hz), 164.8 (d, $J_{C\text{-}F}$ = 248.7 Hz), 169.4 (s), 172.8 (s). Found: C, 61.54; H, 3.21; N, 10.04%. Calcd for $C_{14}H_8F_2N_2S$: C, 61.30; H, 2.94; N, 10.21%.

*3,5-Bis-(p-methoxyphenyl)-1,2,4-thiadiazole (***6d***).* Colorless powder, mp 137–138°C (Lit. [33], 139–140°C).

*3,5-Di-naphthalen-1-yl-1,2,4-thiadiazole (***6e***).* Pale yellow oil; MS *m/z* (%) 338 (M^+; 43), 184 (bp), 153 ($C_{10}H_7CN$, 38); IR (neat) 3062, 2222, 1513, 1375, 1213, 802, 773 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.52 (2H, dd, J = 7.9, 7.5 Hz), 7.61 (2H, dd, J = 7.4, 7.7 Hz), 7.69 (2H, dd, J = 7.9, 7.2 Hz), 7.91 (4H, dd, J = 5.4, 7.0 Hz), 8.07 (2H, d, J = 8.3 Hz), 8.24 (2H, d, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$) δ 117.8 (d), 124.9 (d), 125.1 (d), 127.5 (d), 128.5 (d), 128.6 (d), 132.3 (s), 132.6 (s), 132.9 (s), 133.2 (s), 183.5 (s). Found: C, 78.17; H, 4.13; N, 8.13%. Calcd for $C_{22}H_{14}N_2S$: C, 78.08; H, 4.17; N, 8.28%.

Preparation of 5H-1,2,4-oxathiazole S-Oxides **7** *by mCPBA Oxidation of 5H-1,2,4-oxathiazoles* **5**

A chloroform solution (20 ml) of 5*H*-1,2,4-oxathiazoles (**5**, 1.0 mmol) was treated with *m*CPBA (1.1 mol amt) at 0°C for 1 h in the presence of $NaHCO_3$ (2 mol amt). 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 **7**.

*5-tert-Butyl-3-phenyl-5H-1,2,4-oxathiazole S-Oxide (***7a***).* Pale yellow oil; MS *m/z* (%) 237 (M^+; 3), 221 ($M^+ - O$, 4); 151 ($M^+ - t$-C_4H_9CHO, 84), 57

(t-C_4H_9, bp); IR (neat) 2967, 1655, 1450, 1367, 1130, 952, 792, 770, 689 cm^{-1}; ^1H NMR ($CDCl_3$) major isomer δ 1.06 (9H, s), 6.61 (1H, s), 7.48–7.59 (3H, m), 8.03–8.05 (2H, m), minor isomer δ 1.12 (9H, s), 6.31 (1H, s), 7.48–7.59 (3H, m), 8.03–8.05 (2H, m); ^{13}C NMR ($CDCl_3$) major isomer δ 25.2 (q), 36.1 (s), 109.1 (d), 127.5 (s), 129.3 (d), 130.0 (d), 132.7 (d), 168.9 (s), minor isomer δ 25.8 (q), 36.0 (s), 127.68 (s), 129.2 (d), 129.9 (d), 132.6 (d), 168.2 (s). Found: C, 60.67; H, 6.43; N, 6.01%. Calcd for $C_{12}H_{15}NO_2S$: C, 60.73; H, 6.37; N, 5.90%.

*5-tert-Butyl-3-(p-chlorophenyl)-5H-1,2,4-oxathiazole S-oxide (***7b***).* Pale yellow oil; MS *m/z* (%) 270 ($M^+ - 1$; 1), 201 ($M^+ - t$-C_4H_9CHO, 1); 57 (t-C_4H_9, bp), 29; IR (neat) 2963, 1642, 1594, 1489, 1403, 1132, 1091, 834 cm^{-1}; ^1H NMR ($CDCl_3$) major isomer δ 1.06 (9H, s), 6.59 (1H, s), 7.50 (2H, d, $J = 8.0$ Hz), 7.97 (2H, d, $J = 8.0$ Hz), minor isomer δ 1.12 (9H, s), 6.30 (1H, s), 7.48 (2H, d, $J = 8.0$ Hz), 7.99 (2H, d, $J = 8.0$ Hz); ^{13}C NMR ($CDCl_3$) major isomer δ 25.2 (q), 36.1 (s), 123.9 (d), 125.9 (s), 129.6 (d), 131.1 (d), 139.1 (s), 167.9 (s), minor isomer δ 25.8 (q), 36.2 (s), 125.8 (s), 127.9 (s), 129.5 (d), 131.0 (d), 139.6 (s), 167.2 (s). Found: C, 53.23; H, 5.29; N, 5.12%. Calcd for $C_{12}H_{14}ClNO_2S$: C, 53.38; H, 5.37; N, 5.08%.

*5-tert-Butyl-3-(p-fluorophenyl)-5H-1,2,4-oxathiazole S-oxide (***7c***).* Pale yellow oil; MS *m/z* (%) 256 ($M^+ + 1$; 8), 169 ($M^+ - t$-C_4H_9CHO, 30); IR (neat) 2966, 1644, 1602, 1509, 1160, 1129, 842 cm^{-1}; ^1H NMR ($CDCl_3$) major isomer δ 1.05 (9H, s), 6.59 (1H, s), 7.22 (2H, t, $J = 8.8$ Hz), 8.05–8.10 (2H, m), minor isomer δ 1.12 (9H, s), 6.30 (1H, s), 7.19 (2H, t, $J = 8.6$ Hz), 8.05–8.10 (2H, m); ^{13}C NMR ($CDCl_3$) major isomer δ 25.2 (q), 36.1 (s), 116.3 (dd, $J_{C\text{-}F} = 21.7$ Hz), 123.8 (d, $J_{C\text{-}F} = 2.6$ Hz), 132.2 (s), 132.3 (dd, $J_{C\text{-}F} = 8.7$ Hz), 165.2 (d, $J_{C\text{-}F} = 254.3$ Hz), 167.8 (s), minor isomer δ 25.8 (q), 36.0 (s), 116.2 (dd, $J_{C\text{-}F} = 23.1$ Hz), 123.8 (d, $J_{C\text{-}F} = 2.6$ Hz), 127.9 (br s), 132.2 (d, $J_{C\text{-}F} = 8.7$ Hz), 165.2 (d, $J_{C\text{-}F} = 254.3$ Hz), 168.3 (s). Found: C, 56.32; H, 5.47; N, 5.22%. Calcd for $C_{12}H_{14}FNO_2S$: C, 56.45; H, 5.53; N, 5.49%.

*5-tert-Butyl-3-(p-methoxyphenyl)-5H-1,2,4-oxathiazole S-oxide (***7d***).* Pale yellow oil; MS *m/z* (%) 267 (M^+; 7), 251 ($M^+ - O$; 1), 281 ($M^+ - t$-C_4H_9CHO, 53); 151 (bp); IR (neat) 2963, 2225, 1606, 1511, 1262, 1176, 1127, 1029, 835 cm^{-1}. ^1H NMR ($CDCl_3$) major isomer δ 1.04 (9H, s), 3.87 (3H, s), 6.56 (1H, s), 7.00 (2H, d, $J = 8.8$ Hz), 7.99 (2H, d, $J = 8.5$ Hz), minor isomer δ 1.11 (9H, s), 3.85 (3H, s), 6.27 (1H, s), 6.99 (2H, d, $J = 8.7$ Hz), 8.00 (2H, d, $J = 8.6$ Hz); ^{13}C NMR ($CDCl_3$) major isomer δ 25.2 (q), 36.0 (s), 55.4 (s), 103.9 (d), 114.6 (d), 114.7 (d), 123.9 (s), 131.7 (s), 163.1 (s), minor isomer δ 25.8 (q), 36.0 (s), 55.4 (s), 98.2 (d), 119.8 (s), 127.8 (s), 131.8 (d), 133.8 (d), 168.2 (s); Found: C, 57.92; H, 6.37; N, 5.22%. Calcd for $C_{13}H_{17}NO_3S$: C, 58.40; H, 6.41; N, 5.24%.

*5-tert-Butyl-3-naphthalen-1-yl-5H-1,2,4-oxathiazole S-oxide (***7e***).* Pale yellow oil; MS *m/z* (%) 271 ($M^+ - t$-C_4H_9CHO; 2), 239 ($M^+ - S$; 2); 185 ($M^+ - t$-C_4H_9CHO; 89), 153 ($C_{10}H_7CN$; bp); IR (neat): 2966, 2225, 1639, 1510, 1367, 1129, 1056, 803, 774 cm^{-1}; ^1H NMR ($CDCl_3$) major isomer δ 1.13 (9H, s), 6.77 (1H, s), 7.47–7.51 (3H, m), 7.87–7.93 (1H, m), 8.02–8.06 (1H, m), 8.18–8.23 (1H, m), 9.15 (d, $J = 8.3$ Hz), minor isomer δ 1.22 (9H, s), 6.50 (1H, s), 7.47–7.51 (3H, m), 7.87–7.93 (1H, m), 8.02–8.06 (1H, m), 8.18–8.23 (1H, m), 8.89 (d, $J = 8.3$ Hz); ^{13}C NMR ($CDCl_3$) major isomer δ 25.3 (q), 36.0 (s), 110.1 (d), 124.8 (d), 125.1 (d), 125.6 (s), 127.5 (s), 128.4 (d), 128.5 (d), 128.9 (d), 132.5 (d), 133.2 (d), 133.4 (s), 169.9 (s), minor isomer δ 25.9 (q), 36.4 (s), 110.4 (d), 124.6 (d), 124.8 (d), 125.5 (s), 126.9 (d), 128.3 (s), 131.5 (d), 132.0 (d), 132.3 (d), 132.8 (d), 134.0 (s), 173.6 (s); Found: C, 67.02; H, 6.87; N, 4.52%. Calcd for $C_{17}H_{21}NO_2S$: C, 67.29; H, 6.98; N, 4.62%.

*5-Isopropyl-3-phenyl-5H-1,2,4-oxathiazole S-Oxide (***7f***).* Pale yellow oil; MS *m/z* (%) 223 (M^+; 3), 180 ($M^+ - C_3H_7$; 7), 175 ($M^+ - SO$; 10), 159 ($M^+ - SO_2$; 8), 151 ($M^+ - C_3H_7CHO$; 28), 105 (bp); IR (neat): 2969, 1642, 1473, 1129, 1028, 953, 768, 690 cm^{-1}; ^1H NMR ($CDCl_3$) major isomer δ 1.05 (6H, dd, $J = 6.4$, 6.4 Hz), 2.28 (1H, quint, $J = 4.9$ Hz), 6.73 (1H, d, $J = 4.8$ Hz), 7.43–7.57 (3H, m), 8.03–8.05 (2H, m), minor isomer δ 1.14 (6H, dd, $J = 6.8$, 6.8 Hz), 2.28 (1H, quint, $J = 4.9$ Hz), 6.41 (1H, d, $J = 5.8$ Hz), 7.43–7.57 (3H, m), 8.03–8.05 (2H, m); ^{13}C NMR ($CDCl_3$) major isomer δ 16.9 (q), 18.5 (q), 33.3 (d), 124.8 (d), 129.3 (d), 129.9 (s), 130.3 (d), 132.7 (d), 168.9 (s), minor isomer δ 17.4 (q), 18.0 (q), 34.6 (d), 121.2 (d), 128.3 (s), 128.6 (d), 129.2 (d), 132.6 (d), 166.0 (s); Found: C, 58.02; H, 5.75; N, 6.12%. Calcd for $C_{11}H_{13}NO_2S$: C, 59.17; H, 5.87; N, 6.27%.

Heating of 6H-1,3,5-oxathiazine S-Oxides **4** *in an Ethanol Media*

An ethanol solution (20 ml) of 6*H*-1,3,5-oxathiazine *S*-oxides (**4a**, 1.0 mmol) was heated at refluxing temperature for 26 h. After cooling to room temperature and quenching with water, the reaction mixture was subjected to the usual work up. The crude product was purified using column chromatography on silica

gel to afford 3,5-diphenyl-1,2,4-thiadiazole **6a** (35%), *N*-(1-ethoxy-2,2-dimethylpropyl)thiobenzamide **9a** (12%), along with some unidentified products.

N-(1-ethoxy-2,2-dimethylpropyl)thiobenzamide **9a**. Yellow oil; MS *m/z* (%) 251 (M^+; 50), 222 ($M^+ - C_2H_5$; 84), 87 (bp); IR (neat) 3397, 3290, 2963, 2904, 1501, 1481, 1449, 1370, 1362, 1116, 1069, 961, 736, 693 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (9H, s), 1.21 (3H, br t, $J = 6.9$ Hz), 3.64 (1H, dq, $J = 9.9$, 7.0 Hz), 3.73 (1H, dq, $J = 9.9$, 6.9 Hz), 5.81 (1H, d, $J = 8.0$ Hz), 7.30–7.50 (3H, m), 7.55–7.70 (1H, m), 7.72–7.75 (2H, m); ^{13}C NMR ($CDCl_3$) δ 15.0 (q), 24.9 (q), 36.5 (s), 64.7 (t), 90.4 (d), 126.4 (d), 128.5 (d), 131.1 (d), 142.3 (s), 200.9 (s). Found: C, 66.85; H, 8.76; N, 5.40%. Calcd for $C_{14}H_{21}NOS$: C, 66.89; H, 8.42; N, 5.57%.

X-ray Crystallographic Data for **4d**

Colorless prism of **4d** suitable for X-ray investigation was obtained from $CHCl_3$ at −20°C. Crystal data: $C_{18}H_{27}NO_3S$, FW = 337.48, crystal size $0.15 \times 0.15 \times 0.20$ mm^3, monoclinic, space group $P2_1/n$ (#14), $a = 8.778(2)$, $b = 16.711(4)$, $c = 12.514(3)$ Å, ß = 97.178(5)°, $V = 1821.3(8)$ $Å^3$, $Z = 4$, $D_{calc} = 1.231$ g/cm^3, $\mu = 1.92$ cm^{-1}. From 17055 reflections measured 4129 were unique ($R_{int} = 0.030$). $R = 0.037$, $R_w = 0.040$, MoKα ($\lambda = 0.71070$ Å, $T = -100.0$°C. The structure was solved by direct methods (SIR92). Crystallographic data (excluding structure factors) have been deposited with Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 215096. Copies of the data can be obtained, free of charge, via the Internet http://www.ccdc.cam.ac.uk, or on application to the director; CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Tel. (+44) 1223-336-408; fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk.

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