

## An expedient synthesis of new 2-(furoxan-3-yl)thiazolidin-4-one derivatives

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### Abstract

A series of new biologically interesting furoxan-3-thiazolidinones have been synthesized *via* one-pot three-component reaction of furoxan aldehydes, anilines and mercaptoacetic acid. The multi-component reaction involves condensation of furoxan aldehyde with aniline to give imine; the formed imine undergoes nucleophilic addition with mercaptoacetic acid, followed by cyclisation with loss of H<sub>2</sub>O to obtain the desired products. All the synthesized compounds were well characterized using spectral techniques and confirmed by an X-ray crystal structure for one compound.

**Keywords:** Furoxan-3-carbaldehydes, One-pot reaction, thiazolidin-4-ones, crystal structure

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### Introduction

To fight against disease, society depends on the development of new biologically active compounds. One of the new approaches towards this goal is the development of hybrid heterocyclic compounds. A large number of chemical libraries can be accessed by the combination

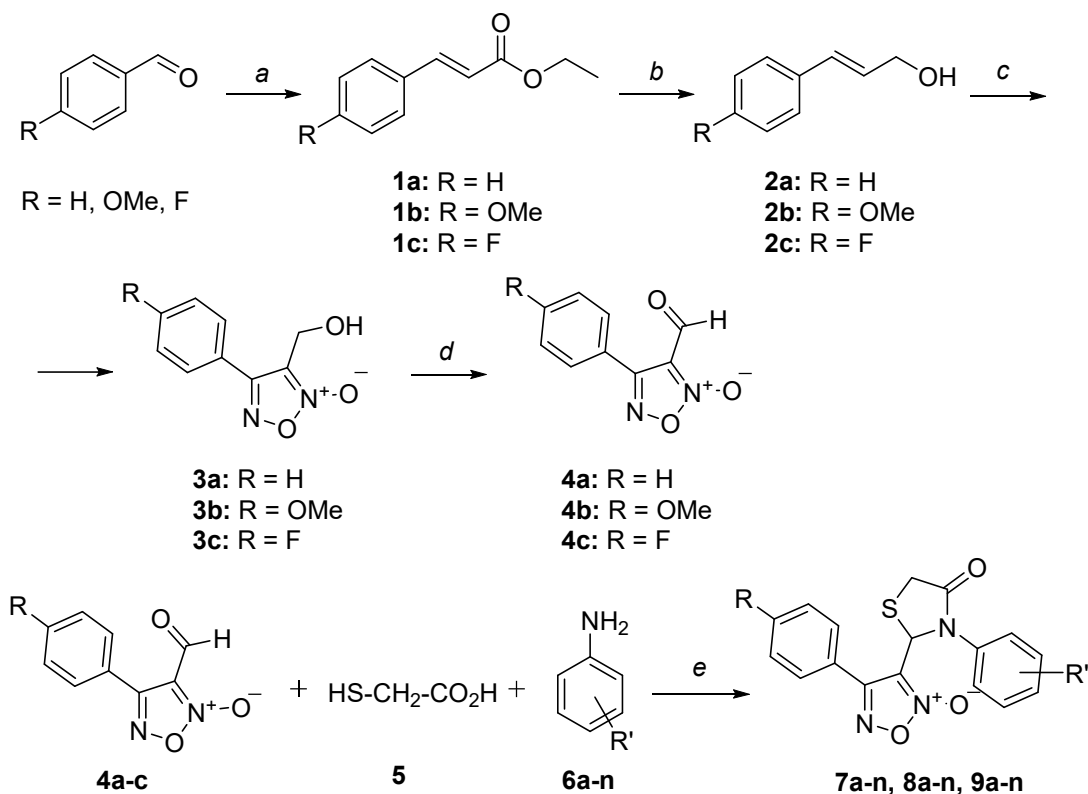
of different heterocycles and they may be considered to be valuable as they incorporate classes of compound with proven utility in medicinal chemistry.

Furoxans (1,2,5-oxadiazole 2-oxides) are a class of five membered heterocyclic compounds having oxygen and nitrogen as heteroatoms. They constitute an important class of heterocyclic compounds possessing biological activities such as antihelmintic, antitumor, antimicrobial, mutagenic, immunosuppressive, anticancer, and anti-aggregating properties.<sup>1-3</sup> Some furoxan derivatives shown potential cardiovascular properties.<sup>4</sup> Furthermore, furoxans are well known as NO-donors, and recently furoxan compounds have shown activity against schistosomiasis.<sup>5</sup> Furoxans are also used in combination with drugs as NO donor-drug hybrids.  $\alpha$ 1-Antagonists,  $\beta$ 1-antagonists,  $\text{Ca}^{2+}$ -channel blockers,  $\text{K}^+$ -channel activators, NSAIDs, and H3- and H2-antagonists are a few examples having NO donor-drug hybrids.<sup>6</sup> NO donor-1,4-dihydropyridine also proved to be  $\text{Ca}^{2+}$ -channel activators.<sup>7</sup> Furthermore, REC15/2739, a uroselective  $\alpha$ 1-antagonist,<sup>8</sup> and Rabeprazole, a potent inhibitor of  $\text{H}^+/\text{K}^+$ -ATPase enzyme,<sup>9</sup> are also NO donor-drugs.

Thiazolidinones and related structures are present in natural products; they have a wide range of biological activities and comprise an important motif in pharmaceutical compounds.<sup>10-13</sup> Thiazolidinones and their derivatives have been reported to possess anticonvulsant,<sup>14-16</sup> antifungal,<sup>17-19</sup> antitubercular,<sup>20,21</sup> antitumour,<sup>22</sup> antiparasitic,<sup>23</sup> herbicidal,<sup>24</sup> anti-inflammatory,<sup>25</sup> analgesic,<sup>26</sup> anticancer,<sup>27,28</sup> antibacterial,<sup>29-31</sup> and antipsychotic<sup>32</sup> properties. They have also been reported to inhibit the bacterial enzyme Mur-B, a precursor in the biosynthesis of peptidoglycon, which is a non-nucleoside inhibitor of HIV-RT.<sup>33,34</sup> Motivated by these findings, and in continuation of our ongoing efforts towards with the discovery of nitrogenated heterocycles with potential chemotherapeutic activities,<sup>35,36</sup> we planned to synthesize a new series of hybrid furoxan-3-thiazolidinone derivatives of potential biological activity.

## Results and Discussion

The present work was designed to synthesize new furoxan-3-thiazolidinones from substituted furoxan aldehydes (**4a-c**). The synthetic scheme was depicted in Scheme 1. The vital intermediates, furoxan aldehydes **4a-c**, were synthesized following a known route from substituted benzaldehydes. Horner Wadsworth Emmons reaction of benzaldehydes in the presence of NaH as a base yielded substituted ethyl cinnamates **1a-c**. The ethyl cinnamates were subjected to DIBAL-H reduction to yield cinnamyl alcohols **2a-c**. Further, the cinnamyl alcohols were treated with aq.  $\text{NaNO}_2$  in the presence of glacial acetic acid to obtain furoxan methanol derivatives **3a-c**.<sup>37</sup> Oxidation of the alcohol functionality of the furoxanmethanols using  $\text{MnO}_2$  yielded furoxan aldehydes **4a-c** in excellent yields.<sup>37</sup> Finally, a one-pot three component reaction of furoxan aldehydes **4a-c** with substituted anilines **6a-n** and mercaptoacetic acid **5** was achieved by simple heating in toluene at 50 °C to obtain the required furoxan-3-thiazolidinones **7a-n**, **8a-n**, **9a-n** in good yields.

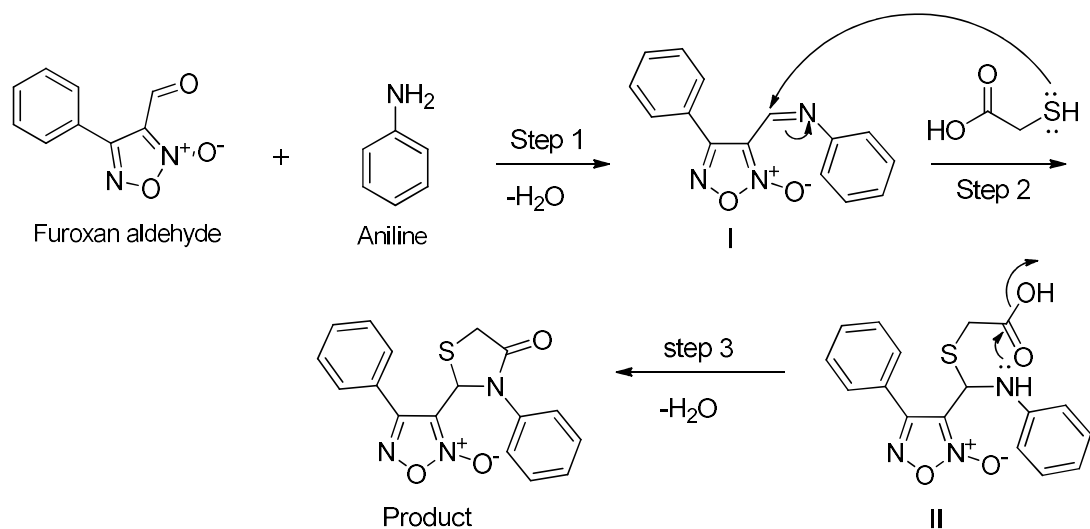


*Reagents and conditions:* *a*  $(\text{EtO})_2\text{P}(\text{O})\text{CH}_2\text{COOEt}$ , NaH, DCM, 0 °C-rt, 1 h, 85-90%.  
*b* DIBAL-H, DCM, 0 °C, 4 h. *c* Acetic acid, aq.  $\text{NaNO}_2$ , rt, 4-6 h, 30-75%. *d*  $\text{MnO}_2$ ,  $\text{CH}_2\text{Cl}_2$ , 2-4h, 85-95% *e* Toluene, 50 °C, 4 h, 70-84%.

**Scheme 1.** The preparation of furoxanyl thiazolidinones **7-9**.

Multi-component reaction (MCR) involves three main steps. In step 1, the condensation of furoxan aldehyde with aniline forms imine I; the imine undergoes nucleophilic addition with mercaptoacetic acid to give intermediate II (step 2), followed by cyclisation (by loss of  $\text{H}_2\text{O}$ ) to give the final product (step 3) as shown in Scheme 2. All the synthesized compounds are listed in Table 1.

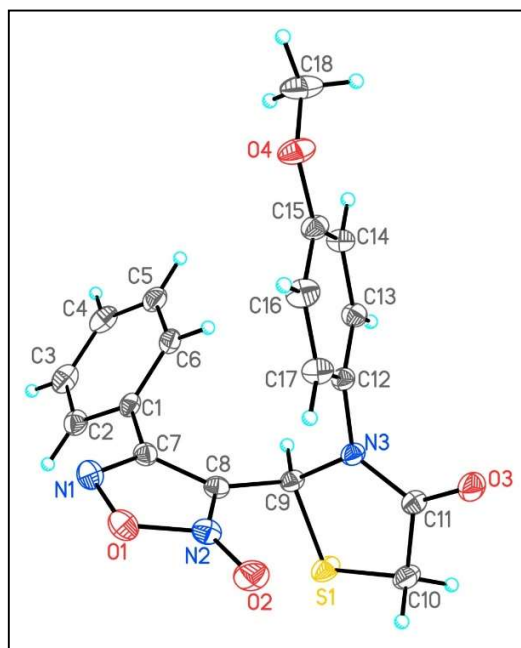
The structural connectivity of the furoxan thiazolidinones is confirmed by a single-crystal X-ray diffraction analysis of compound **7g**, as shown in Figure 1.



**Scheme 2.** Suggested pathway to thiazolidinone ring formation.

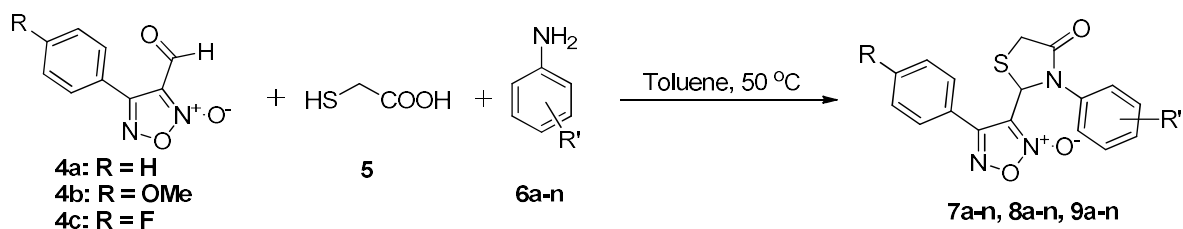
### X-ray Crystallographic analysis<sup>38,39</sup>

Data for **7g**, a colorless crystal compound, molecular weight:  $C_{18}H_{15}N_3O_4S$ ,  $M = 369.394$ , colorless block,  $0.38 \times 0.34 \times 0.26 \text{ mm}^3$ , monoclinic, space group  $P2_1/n$  (No. 14),  $a = 8.9714(7)$ ,  $b = 16.3622(13)$ ,  $c = 11.8077(9) \text{ \AA}$ ,  $\beta = 98.4520(10)^\circ$ ,  $V = 1714.4(2) \text{ \AA}^3$ ,  $Z = 4$ ,  $D_c = 1.431 \text{ g/cm}^3$ ,  $F_{000} = 768$ , CCD area detector, MoK $\alpha$  radiation,  $\lambda = 0.71073 \text{ \AA}$ ,  $T = 293(2) \text{ K}$ ,  $2\theta_{\text{max}} = 50.0^\circ$ , 16244 reflections collected, 3020 unique ( $R_{\text{int}} = 0.0192$ ), Final  $Goof = 1.030$ ,  $RI = 0.0312$ ,  $wR2 = 0.0845$ ,  $R$  indices based on 2767 reflections with  $I > 2\sigma(I)$  (refinement on  $F^2$ ), 237 parameters,  $\mu = 0.219 \text{ mm}^{-1}$ .



**Figure 1.** ORTEP diagram of the compound **7g**.

**Table 1.** One-pot synthesis of 2-(furoxan-3-yl)thiazolidin-4-ones



Entry	Furoxan aldehyde	Substituted Aniline	Product	Isolated yield (%)	Melting point (°C)
1	<b>4a</b>	R'=H ( <b>6a</b> )	R, R' = H ( <b>7a</b> )	82	82-84
2	<b>4a</b>	R'=4- <i>n</i> -Bu ( <b>6b</b> )	R=H; R'= 4- <i>n</i> -Bu ( <b>7b</b> )	77	100-102
3	<b>4a</b>	R'=4- <i>i</i> -Pr ( <b>6c</b> )	R=H; R'=4- <i>i</i> -Pr ( <b>7c</b> )	75	160-164
4	<b>4a</b>	R'=4- <i>t</i> -Bu ( <b>6d</b> )	R=H; R'=4- <i>t</i> -Bu ( <b>7d</b> )	81	150-152
5	<b>4a</b>	R'=3,5-diMe ( <b>6e</b> )	R=H; R'=3,5-diMe ( <b>7e</b> )	78	160-161
6	<b>4a</b>	R'=3,4-diMe ( <b>6f</b> )	R=H; R'=3,4-diMe ( <b>7f</b> )	78	145-147
7	<b>4a</b>	R'=4-OMe ( <b>6g</b> )	R=H; R'=4-OMe ( <b>7g</b> )	78	129-131
8	<b>4a</b>	R'=3,4-diOMe ( <b>6h</b> )	R=H; R'=3,4-diOMe ( <b>7h</b> )	77	120-124
9	<b>4a</b>	R'=3,4-OCH <sub>2</sub> O ( <b>6i</b> )	R=H; R'=3,4-OCH <sub>2</sub> O ( <b>7i</b> )	77	121-123
10	<b>4a</b>	R'=3-F ( <b>6j</b> )	R=H; R'=3-F ( <b>7j</b> )	77	99-101

Table 1 (continued)

Entry	Furoxan aldehyde	Substituted Aniline	Product	Isolated yield (%)	Melting point (°C)
11	<b>4a</b>	R'=4-F ( <b>6k</b> )	R=H; R'=4-F ( <b>7k</b> )	77	118-120
12	<b>4a</b>	R'=3-Cl ( <b>6l</b> )	R=H; R'=3-Cl ( <b>7l</b> )	80	108-110
13	<b>4a</b>	R'=4-Cl ( <b>6m</b> )	R=H; R'=4-Cl ( <b>7m</b> )	81	158-159
14	<b>4a</b>	R'=4-Br ( <b>6n</b> )	R=H; R'=4-Br ( <b>7n</b> )	70	198-200
15	<b>4b</b>	R'=H ( <b>6a</b> )	R=OMe R' = H ( <b>8a</b> )	80	150-152
16	<b>4b</b>	R'= 4- <i>n</i> -Bu ( <b>6b</b> )	R= OMe; R'= 4- <i>n</i> -Bu ( <b>8b</b> )	81	99-100
17	<b>4b</b>	R'=4- <i>i</i> -Pr ( <b>6c</b> )	R= OMe; R'=4- <i>i</i> -Pr ( <b>8c</b> )	77	125-127
18	<b>4b</b>	R'=4- <i>t</i> -Bu ( <b>6d</b> )	R= OMe; R'=4- <i>t</i> -Bu ( <b>8d</b> )	81	126-128
19	<b>4b</b>	R'=3,5-diMe ( <b>6e</b> )	R= OMe; R'=3,5-diMe ( <b>8e</b> )	84	128-130
20	<b>4b</b>	R'=3,4-diMe ( <b>6f</b> )	R= OMe; R'=3,4-diMe ( <b>8f</b> )	78	120-122
21	<b>4b</b>	R'=4-OMe ( <b>6g</b> )	R= OMe; R'=4-OMe ( <b>8g</b> )	78	112-114
22	<b>4b</b>	R'=3,4-diOMe ( <b>6h</b> )	R= OMe; R'=3,4-diOMe ( <b>8h</b> )	78	128-130
23	<b>4b</b>	R'=3,4-OCH <sub>2</sub> O ( <b>6i</b> )	R= OMe; R'=3,4-OCH <sub>2</sub> O ( <b>8i</b> )	76	165-168
24	<b>4b</b>	R'=3-F ( <b>6j</b> )	R= OMe; R'=3-F ( <b>8j</b> )	74	120-122
25	<b>4b</b>	R'=4-F ( <b>6k</b> )	R= OMe; R'=4-F ( <b>8k</b> )	74	110-112
26	<b>4b</b>	R'=3-Cl ( <b>6l</b> )	R= OMe; R'=3-Cl ( <b>8l</b> )	76	125-128
27	<b>4b</b>	R'=4-Cl ( <b>6m</b> )	R= OMe; R'=4-Cl ( <b>8m</b> )	77	123-125
28	<b>4b</b>	R'=4-Br ( <b>6n</b> )	R= OMe; R'=4-Br ( <b>8n</b> )	70	122-124
29	<b>4c</b>	R'=H ( <b>6a</b> )	R=F; R' = H ( <b>9a</b> )	82	108-110
30	<b>4c</b>	R'=4- <i>n</i> -Bu ( <b>6b</b> )	R=F; R'=4- <i>n</i> -Bu ( <b>9b</b> )	78	90-93
31	<b>4c</b>	R'=4- <i>i</i> -Pr ( <b>6c</b> )	R=F; R'=4- <i>i</i> -Pr ( <b>9c</b> )	78	160-161
32	<b>4c</b>	R'=4- <i>t</i> -Bu ( <b>6d</b> )	R=F; R'=4- <i>t</i> -Bu ( <b>9d</b> )	76	175-178
33	<b>4c</b>	R'=3,5-diMe ( <b>6e</b> )	R=F; R'=3,5-diMe ( <b>9e</b> )	76	178-180
34	<b>4c</b>	R'=3,4-diMe ( <b>6f</b> )	R=F; R'=3,4-diMe ( <b>9f</b> )	79	145-147
35	<b>4c</b>	R'=4-OMe ( <b>6g</b> )	R=F; R'=4-OMe ( <b>9g</b> )	77	142-144
36	<b>4c</b>	R'=3,4-diOMe ( <b>6h</b> )	R=F; R'=3,4-diOMe ( <b>9h</b> )	77	160-163
37	<b>4c</b>	R'=3,4-OCH <sub>2</sub> O ( <b>6i</b> )	R=F; R'=3,4-OCH <sub>2</sub> O ( <b>9i</b> )	74	180-182
38	<b>4c</b>	R'=3-F ( <b>6j</b> )	R=F; R'=3-F ( <b>9j</b> )	73	128-131
39	<b>4c</b>	R'=4-F ( <b>6k</b> )	R=F; R'=4-F ( <b>9k</b> )	74	148-150
40	<b>4c</b>	R'=3-Cl ( <b>6l</b> )	R=F; R'=3-Cl ( <b>9l</b> )	74	105-107
41	<b>4c</b>	R'=4-Cl ( <b>6m</b> )	R=F; R'=4-Cl ( <b>9m</b> )	82	109-110
42	<b>4c</b>	R'=4-Br ( <b>6n</b> )	R=F; R'=4-Br ( <b>9n</b> )	70	147-150

## Conclusions

Syntheses of a number of new furoxan-3-thiazolidinones were successfully accomplished and are well characterized by spectral data. The anticancer activity of these compounds is being studied and will be reported in due course.

## Experimental Section

**General.** All reactions involving air-sensitive reagents were performed under nitrogen atmosphere. Solvents were freshly dried and purified by conventional methods prior to use. The progress of all the reactions was monitored by TLC, using TLC aluminium sheets precoated with silica gel 60 F<sub>254</sub> to a thickness of 0.25 mm (Merck). Flash column chromatography was done using silica gel (Merck, 60-120 mesh). Melting points were determined on a MEL-TEMP II melting point apparatus. IR spectra were recorded on a Perkin-Elmer FT-IR spectrophotometer and expressed with ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ). <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Varian Gemini 200 MHz, Bruker Avance 300 MHz spectrometer; TMS was used as an internal standard in CDCl<sub>3</sub>/DMSO-d<sub>6</sub>. Mass spectra were recorded on VG Micromass 7070 H (EI), QSTAR XL High resolution mass spectrometer (HRMS), Thermofinnigan ESI ion trap Mass Spectrometer and a GC-MS system on an Agilent 6890 series.

**Furoxan aldehydes 4a-c:** these were prepared as described.<sup>37</sup> Compound **4a**, mp 65-66 °C (lit. mp 64-65 °C); **4b**, mp 92-94 °C; **4c**, 74-76 °C (no lit.<sup>37</sup> mps were reported for **4b,c**).

**General procedure for the preparation of furoxan-3-thiazolidinones.** To the solution of furoxan aldehyde (2.5 mmol) in 10 mL toluene, was added aniline (2.75 mmol) in 10 mL of toluene at 0 °C. After formation of imine which is monitored by TLC, thioglycolic acid (10 mmol) was added to the reaction mixture at the same temperature. The reaction was stirred and heated at 50 °C for 4 h. After completion of the reaction, the reaction mixture was diluted with ethyl acetate and washed with saturated solution of NaHCO<sub>3</sub> (3 × 20 mL). The combined organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>), concentrated under reduced pressure. The crude products were purified using silica-gel column chromatography (eluent-3:2 hexane-ethyl acetate), to afford pure products.

**3-(4-Oxo-3-phenylthiazolidin-2-yl)-4-phenyl-1,2,5-oxadiazole 2-oxide (7a).** White solid (82%), m.p. 82-84 °C, IR (film): 2924, 2853, 1703, 1596, 1492, 1455, 1377, 1218, 834, 770  $\text{cm}^{-1}$ . <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.60-7.45 (m, 3H), 7.40-7.24 (m, 5H), 7.16-7.10 (m, 2H), 6.17 (s, 1H), 4.04 (brd, 1H, *J* 15.2 Hz), 3.77 (d, 1H, *J* 15.2 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  170.1, 155.7, 136.0, 131.3, 129.7, 129.2, 128.4, 127.9, 125.3, 125.1, 114.4, 54.6, 33.7. ESI-MS: *m/z* 362 (M+Na)<sup>+</sup>. HRMS (ESI): *m/z* [M + Na]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>13</sub>N<sub>3</sub>O<sub>3</sub>SNa: 362.0570; Found: 362.0588.

**3-[3-(4-Butylphenyl)-4-oxothiazolidin-2-yl]-4-phenyl-1,2,5-oxadiazole 2-oxide (7b).** White solid (77%), m.p. 100-102 °C, IR (film): 3036, 2927, 2856, 1693, 1594, 1453, 1341, 782, 759  $\text{cm}^{-1}$ .

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.55 (tt, 1H, *J* 7.4, 1.8 Hz), 7.50-7.45 (m, 2H), 7.24 (brd, 2H, *J* 7.4 Hz), 7.16 (dd, 2H, *J* 8.3 Hz), 7.02 (dd, 2H, *J* 8.3 Hz), 6.11 (s, 1H), 4.02 (brd, 1H, *J* 15.1 Hz), 3.74 (d, 1H, *J* 15.1 Hz), 2.57 (t, 2H, *J* 7.7 Hz), 1.62-1.52 (m, 2H), 1.36-1.26 (m, 2H), 0.90 (t, 3H, *J* 7.3 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.2, 155.8, 143.6, 133.5, 131.3, 129.7, 129.2, 128.0, 125.3, 125.2, 114.4, 54.8, 35.1, 33.7, 33.2, 22.1, 13.8. ESI-MS: *m/z* 396 (M+H)<sup>+</sup>. HRMS (ESI): *m/z* [M + H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>22</sub>N<sub>3</sub>O<sub>3</sub>S: 396.1376; Found: 396.1380.

**3-[3-(4-Isopropylphenyl)-4-oxothiazolidin-2-yl]-4-phenyl-1,2,5-oxadiazole 2-oxide (7c).** White solid (75%), m.p. 160-164 °C, IR (film): 3385, 2964, 2368, 1701, 1591, 1224, 700 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.63-7.44 (m, 3H), 7.29-7.17 (m, 4H), 7.03 (d, 2H, *J* 8.3 Hz), 6.10 (s, 1H), 4.02 (brd, 1H, *J* 15.1 Hz), 3.74 (d, 1H, *J* 15.1 Hz), 2.88 (sept, 1H, *J* 6.7 Hz), 1.21 (d, 6H, *J* 6.7 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.2, 155.8, 149.4, 133.5, 131.2, 129.2, 128.0, 127.8, 125.4, 125.2, 114.4, 54.7, 33.7 (2C), 23.7. ESI-MS: *m/z* 382 (M+H)<sup>+</sup>. HRMS (ESI): *m/z* [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>20</sub>N<sub>3</sub>O<sub>3</sub>S: 382.1225; Found: 382.1229.

**3-[3-(4-*tert*-Butylphenyl)-4-oxothiazolidin-2-yl]-4-phenyl-1,2,5-oxadiazole 2-oxide (7d).** White solid (81%), m.p. 150-152 °C, IR (film): 3000, 2964, 2870, 1702, 1594, 772, 625 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.56 (tt, 1H, *J* 7.4, 1.8 Hz), 7.50-7.45 (m, 2H), 7.38-7.36 (m, 2H), 7.21 (brd, 2H, *J* 7.1 Hz), 7.06-7.03 (m, 2H), 6.11 (s, 1H), 4.01 (brs, 1H), 3.75 (d, 1H, *J* 15.1 Hz), 1.28 (s, 9H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.5, 155.8, 151.7, 133.0, 131.2, 129.1, 127.9, 126.6, 125.1, 125.0, 114.4, 64.0, 49.9, 30.9, 24.8. ESI-MS: *m/z* 396 (M+Na)<sup>+</sup>. HRMS (ESI): *m/z* [M + H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>22</sub>N<sub>3</sub>O<sub>3</sub>S: 396.1379; Found: 396.1376.

**3-[3-(3,5-Dimethylphenyl)-4-oxothiazolidin-2-yl]-4-phenyl-1,2,5-oxadiazole 2-oxide (7e).** White solid (78%), m.p. 160-161 °C, IR (film): 2921, 2852, 1681, 1598, 1384, 1217, 1024, 860, 768 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.57 (tt, 1H, *J* 7.6, 1.8 Hz), 7.49 (m, 2H), 7.27 (brd, 2H, *J* 7.2 Hz), 6.92 (s, 1H), 6.70 (s, 2H), 6.13 (s, 1H), 4.05 (brd, 1H, *J* 14.6 Hz), 3.75 (d, 1H, *J* 14.6 Hz), 2.23 (s, 6H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.1, 155.9, 139.6, 135.8, 131.3, 130.3, 129.3, 128.1, 125.4, 123.1, 114.5, 54.8, 33.9, 21.2. ESI-MS: *m/z* 390 (M+Na)<sup>+</sup>. HRMS (ESI): *m/z* [M + H]<sup>+</sup> Calcd for C<sub>19</sub>H<sub>18</sub>N<sub>3</sub>O<sub>3</sub>S: 368.1063; Found: 368.1056.

**3-[3-(3,4-Dimethylphenyl)-4-oxothiazolidin-2-yl]-4-phenyl-1,2,5-oxadiazole 2-oxide (7f).** White solid (78%), m.p. 145-147 °C, IR (film): 3421, 2922, 1594, 1136, 785, 631 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.59-7.55 (m, 1H), 7.49 (t, 2H, *J* 7.4 Hz), 7.28 (d, 2H, *J* 7.0 Hz), 7.11 (d, 1H, *J* 8.2 Hz), 6.87-6.84 (m, 2H), 6.13 (s, 1H), 3.75 (d, 1H, *J* 15.2 Hz), 2.22 (s, 3H), 2.18 (s, 3H), 4.02 (brs, 1H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.1, 155.8, 138.3, 137.3, 133.5, 131.2, 130.7, 129.2, 128.0, 126.5, 125.3, 122.6, 114.4, 54.7, 33.8, 19.7, 19.4. ESI-MS: *m/z* 390 (M+Na)<sup>+</sup>. HRMS (ESI): *m/z* [M + Na]<sup>+</sup> Calcd for C<sub>19</sub>H<sub>17</sub>N<sub>3</sub>O<sub>3</sub>SNa: 390.0890; Found: 390.0889.

**3-[3-(4-Methoxyphenyl)-4-oxothiazolidin-2-yl]-4-phenyl-1,2,5-oxadiazole 2-oxide (7g).** Brown solid (78%), m.p. 129-131 °C, IR (film): 2922, 2851, 1693, 1594, 1235, 1017, 840, 766, 699 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.61-7.54 (m, 1H), 7.53-7.46 (m, 2H), 7.30-7.24 (m, 2H), 7.05 (d, 2H, *J* 8.7 Hz), 6.87 (d, 2H, *J* 8.7 Hz), 6.08 (s, 1H), 4.05 (brd, 1H, *J* 13.9 Hz), 3.76 (d, 1H, *J* 13.9 Hz), 3.78 (s, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.3, 159.3, 155.7, 131.2, 129.2, 128.4,



127.9, 127.0, 125.1, 114.9, 114.3, 55.3, 54.8, 33.6. ESI-MS:  $m/z$  370 (M+H)<sup>+</sup>. HRMS (ESI):  $m/z$  [M + H]<sup>+</sup> Calcd for C<sub>18</sub>H<sub>16</sub>N<sub>3</sub>O<sub>4</sub>S: 370.0856; Found: 370.0860.

**3-[3-(3,4-Dimethoxyphenyl)-4-oxothiazolidin-2-yl]-4-phenyl-1,2,5-oxadiazole 2-oxide (7h).**

White solid (77%), m.p. 120-124 °C, IR (film): 2926, 1692, 1585, 1216, 1017, 936, 768, 682 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.60-7.45 (m, 3H), 7.28 (d, 2H, *J* 7.5 Hz), 6.81 (d, 1H, *J* 8.4Hz), 6.68 (dd, 1H, *J* 8.4, 2.2 Hz), 6.61 (d, 1H, *J* 2.2 Hz), 6.11 (s, 1H), 4.06 (brd, 1H, *J* 14.9 Hz), 3.86 (s, 3H), 3.77 (d, 1H, *J* 14.9), 3.74 (s, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.2, 155.7, 149.6, 149.0, 131.3, 129.3, 128.7, 128.0, 125.3, 118.0, 114.4, 111.4, 108.9, 55.9, 55.9, 54.8, 33.7. ESI-MS:  $m/z$  400 (M+H)<sup>+</sup>. HRMS (ESI):  $m/z$  [M + H]<sup>+</sup> Calcd for C<sub>19</sub>H<sub>18</sub>N<sub>3</sub>O<sub>5</sub>S: 400.0958; Found: 400.0955.

**3-[3-(1,3-Benzodioxol-5-yl)-4-oxothiazolidin-2-yl]-4-phenyl-1,2,5-oxadiazole 2-oxide (7i).**

White solid (77%), m.p. 121-123 °C, IR (film): 3003, 2965, 2930, 1697, 1591, 833, 779 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.58 (tt, 1H, *J* 1.9, 7.4 Hz), 7.53-7.49 (m, 2H), 7.32 (brd, 2H, *J* 7.3 Hz), 6.76 (d, 1H, *J* 8.2 Hz), 6.63 (d, 1H, *J* 1.9 Hz), 6.57 (dd, 1H, *J* 8.2, 1.9 Hz), 6.05 (s, 1H), 5.99-5.98 (m, 2H), 4.04 (brd, 1H, *J* 15.2 Hz), 3.75 (d, 1H, *J* 15.2 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.4, 155.6, 148.5, 147.7, 131.3, 129.5, 129.3, 127.9, 125.1, 119.4, 114.3, 108.6, 107.1, 101.8, 64.2, 33.6. ESI-MS:  $m/z$  384 (M+H)<sup>+</sup>. HRMS (ESI):  $m/z$  [M + H]<sup>+</sup> Calcd for C<sub>18</sub>H<sub>14</sub>N<sub>3</sub>O<sub>5</sub>S: 384.0648; Found: 384.0658.

**3-[3-(3-Fluorophenyl)-4-oxothiazolidin-2-yl]-4-phenyl-1,2,5-oxadiazole 2-oxide (7j).**

Brown solid (77%), m.p. 99-101 °C, IR (film): 2924, 1595, 1376, 1020 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.60 (tt, 1H, *J* 7.3, 1.3 Hz), 7.56-7.51 (m, 2H), 7.33 (brd, 2H, *J* 8.2 Hz), 7.32-7.29 (m, 1H), 7.00 (dt, 1H, *J* 7.4, 1.8 Hz), 6.94-6.89 (m, 2H), 6.19 (s, 1H), 3.99 (brd, 1H, *J* 15.4 Hz), 3.77 (d, 1H, *J* 15.4 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 169.9, 162.8 (d, *J* 249.2 Hz), 155.6, 137.5 (d, *J* = 9.9 Hz), 131.4, 130.8 (d, *J* = 8.8 Hz), 129.4, 128.0, 125.1, 120.1, 115.3 (d, *J* 21.5 Hz), 114.4, 112.6 (d, *J* 24.2 Hz), 54.4, 33.7. ESI-MS:  $m/z$  358 (M+H)<sup>+</sup>. HRMS (ESI):  $m/z$  [M + H]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>13</sub>FN<sub>3</sub>O<sub>3</sub>S: 358.0656; Found: 358.0661.

**3-[3-(4-Fluorophenyl)-4-oxothiazolidin-2-yl]-4-phenyl-1,2,5-oxadiazole 2-oxide (7k).**

White solid (77%), m.p. 118-120 °C, IR (film): 3019, 2927, 1697, 1598, 1509, 1383, 1217, 825, 767 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.62-7.48 (m, 3H), 7.29 (brd, 2H, *J* 7.5 Hz), 7.14-7.00 (m, 4H), 6.13 (s, 1H), 4.04 (brd, 1H, *J* 15.1 Hz), 3.77 (d, 1H, *J* 15.1 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.2, 161.8 (d, *J* 248.8 Hz), 155.6, 131.9 (d, *J* 2.7 Hz), 131.4, 129.4, 127.9, 127.5 (d, *J* 9.1 Hz), 125.1, 116.9 (d, *J* 24.7 Hz), 114.2, 54.6, 33.6. ESI-MS:  $m/z$  358 (M+H)<sup>+</sup>. HRMS (ESI):  $m/z$  [M + H]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>13</sub>FN<sub>3</sub>O<sub>3</sub>S: 358.0656; Found: 358.0660.

**3-[3-(3-Chlorophenyl)-4-oxothiazolidin-2-yl]-4-phenyl-1,2,5-oxadiazole 2-oxide (7l).**

White solid (80%), m.p. 108-110 °C, IR (film): 2922, 2852, 1697, 1593, 1387, 1019, 769, 723, 692 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.63-7.50 (m, 3H), 7.32 (brd, 2H, *J* 6.9 Hz), 7.29-7.25 (m, 2H), 7.11 (s, 1H), 7.06-7.01 (m, 1H), 6.18 (s, 1H), 4.02 (brd, 1H, *J* 15.4 Hz), 3.76 (d, 1H, *J* 15.4 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 169.9, 155.6, 137.1, 135.1, 131.4, 130.5, 129.4, 128.3, 128.0, 125.3, 125.1, 122.8, 114.2, 54.3, 33.6. ESI-MS:  $m/z$  374, (M+H)<sup>+</sup>. HRMS (ESI):  $m/z$  [M + H]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>13</sub><sup>35</sup>ClN<sub>3</sub>O<sub>3</sub>S: 374.0360; Found: 374.0369; Calcd for C<sub>17</sub>H<sub>13</sub><sup>37</sup>ClN<sub>3</sub>O<sub>3</sub>S: 376.0332; Found: 376.0336.

**3-[3-(4-Chlorophenyl)-4-oxothiazolidin-2-yl]-4-phenyl-1,2,5-oxadiazole 2-oxide (7m).** White solid (81%), m.p. 158-159 °C, IR (film): 2924, 2853, 1697, 1575, 1387, 761, 722  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.59 (tt, 1H,  $J$  7.4, 1.3 Hz), 7.55-7.51 (m, 2H), 7.34-7.30 (m, 4H), 7.07 (d, 2H,  $J$  8.6 Hz), 6.17 (s, 1H), 4.00 (brd, 1H,  $J$  15.2), 3.76 (d, 1H,  $J$  15.2 Hz).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  170.0, 155.7, 137.1, 131.6, 130.7, 129.5, 128.5, 128.1, 125.4, 125.1, 123.0, 114.3, 54.4, 33.8. ESI-MS:  $m/z$  374, (M+H) $^+$ . HRMS (ESI):  $m/z$  [M+H] $^+$  Calcd for  $\text{C}_{17}\text{H}_{13}^{35}\text{ClN}_3\text{O}_3\text{S}$ : 374.0360; Found: 374.0370; Calcd for  $\text{C}_{17}\text{H}_{13}^{37}\text{ClN}_3\text{O}_3\text{S}$ : 376.0332; Found: 376.0335.

**3-[3-(4-Bromophenyl)-4-oxothiazolidin-2-yl]-4-phenyl-1,2,5-oxadiazole 2-oxide (7n).** Yellowish white solid (70%), m.p. 198-200 °C, IR (film): 3515, 3047, 2349, 1694, 1510, 1258, 1031  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.63-7.58 (m, 1H), 7.55-7.51 (m, 2H), 7.47 (d, 2H,  $J$  8.6 Hz), 7.35-7.32 (m, 2H), 7.01 (d, 2H,  $J$  8.6 Hz), 6.18 (s, 1H), 4.00 (brd, 1H,  $J$  15.2 Hz), 3.76 (d, 1H,  $J$  15.2 Hz).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  170.0, 155.6, 135.0, 132.8, 131.5, 129.4, 128.0, 126.6, 125.1, 122.0, 114.3, 54.3, 33.7. ESI-MS:  $m/z$  419 (M+H) $^+$ . HRMS (ESI):  $m/z$  [M + H] $^+$  Calcd for  $\text{C}_{17}\text{H}_{13}^{79}\text{BrN}_3\text{O}_3\text{S}$ : 417.9856; Found: 417.9869; Calcd for  $\text{C}_{17}\text{H}_{13}^{81}\text{BrN}_3\text{O}_3\text{S}$ : 419.9841; Found: 419.9842.

**4-(4-Methoxyphenyl)-3-(4-oxo-3-phenylthiazolidin-2-yl)-1,2,5-oxadiazole 2-oxide (8a).** White solid (80%), m.p. 150-152 °C, IR (film): 3010, 2934, 2837, 1696, 1597, 1446, 1022, 838, 745  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.60-7.46 (m, 3H), 7.30-7.24 (m, 2H), 7.05 (d, 2H,  $J$  8.7 Hz), 6.87 (d, 2H,  $J$  8.7 Hz), 6.08 (s, 1H), 4.05 (brd, 1H,  $J$  13.8 Hz), 3.78 (s, 3H), 3.76 (d, 1H,  $J$  13.8 Hz).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  170.1, 161.9, 155.5, 136.1, 129.7, 129.5, 128.3, 125.3, 117.3, 114.7, 114.4, 55.4, 54.7, 33.8. ESI-MS:  $m/z$  370 (M+H) $^+$ . HRMS (ESI):  $m/z$  [M + H] $^+$  Calcd for  $\text{C}_{18}\text{H}_{16}\text{N}_3\text{O}_4\text{S}$ : 370.0856; Found: 370.0858.

**3-[3-(4-butylphenyl)-4-oxothiazolidin-2-yl]-4-(4-methoxyphenyl)-1,2,5-oxadiazole 2-oxide (8b).** White solid (81%), m.p. 99-100 °C, IR (film): 2958, 2933, 2856, 1691, 1596, 1448, 1252, 838, 781  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.22-7.13 (m, 4H), 7.02 (d, 2H,  $J$  8.3 Hz), 5.97 (d, 2H,  $J$  8.3 Hz), 6.12 (s, 1H), 4.06 (brd, 1H,  $J$  15.1 Hz), 3.86 (s, 3H), 3.75 (d, 1H,  $J$  15.1 Hz), 2.57 (t, 2H,  $J$  7.5 Hz), 1.66-1.50 (m, 2H), 1.38-1.25 (m, 2H), 0.90 (t, 3H,  $J$  6.9 Hz).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  170.2, 161.8, 155.5, 143.5, 133.5, 129.7, 129.5, 125.4, 117.4, 114.7, 114.4, 55.4, 54.8, 35.1, 33.8, 33.2, 22.2, 13.8. ESI-MS:  $m/z$  448 (M+Na) $^+$ . HRMS (ESI):  $m/z$  [M + H] $^+$  Calcd for  $\text{C}_{22}\text{H}_{24}\text{N}_3\text{O}_4\text{S}$ : 426.1482; Found: 426.1480.

**3-[3-(4-Isopropylphenyl)-4-oxothiazolidin-2-yl]-4-(4-methoxyphenyl)-1,2,5-oxadiazole 2-oxide (8c).** White solid (77%), m.p. 125-127 °C, IR (film): 3318, 2684, 1539, 1285, 1057, 757  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.29-7.14 (m, 4H), 7.04 (d, 2H,  $J$  8.3 Hz), 6.97 (d, 2H,  $J$  8.3 Hz), 6.12 (s, 1H), 4.05 (brd, 1H,  $J$  15.1 Hz), 3.86 (s, 3H), 3.76 (d, 1H,  $J$  15.1 Hz), 2.88 (sept, 1H,  $J$  7.5 Hz), 1.21 (d, 6H,  $J$  7.5 Hz).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  170.2, 161.8, 155.6, 149.4, 133.6, 129.5, 127.8, 125.4, 117.3, 114.7, 114.5, 55.4, 54.8, 33.8, 33.7, 23.7. ESI-MS:  $m/z$  412 (M+H) $^+$ . HRMS (ESI):  $m/z$  [M + H] $^+$  Calcd for  $\text{C}_{21}\text{H}_{22}\text{N}_3\text{O}_4\text{S}$ : 412.1312; Found: 412.1316.

**3-[3-(4-tert-Butylphenyl)-4-oxothiazolidin-2-yl]-4-(4-methoxyphenyl)-1,2,5-oxadiazole 2-oxide (8d).** White solid (81%), m.p. 126-128 °C, IR (film): 3369, 2930, 1697, 1591, 1252, 1091, 833  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.37 (d, 2H,  $J$  8.5 Hz), 7.17 (brs, 2H), 7.05 (d, 2H,  $J$  8.5

Hz), 6.97 (d, 2H, *J* 8.6 Hz), 6.12 (s, 1H), 4.04 (brs, 1H), 3.89 (s, 3H), 3.75 (d, 1H, *J* 15.2 Hz), 1.28 (s, 9H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.2, 161.8, 155.6, 151.6, 133.3, 129.5, 126.7, 114.7, 117.4, 114.5, 125.0, 55.4, 54.8, 34.6, 33.8, 31.1. ESI-MS: *m/z* 426 [M+H]<sup>+</sup>. HRMS (ESI): *m/z* [M + H]<sup>+</sup> Calcd for C<sub>22</sub>H<sub>24</sub>N<sub>3</sub>O<sub>4</sub>S: 426.1482; Found: 426.1484.

**3-[3-(3,5-Dimethylphenyl)-4-oxothiazolidin-2-yl]-4-(4-methoxyphenyl)-1,2,5-oxadiazole 2-oxide (8e).** White solid (84%), m.p. 128-130 °C, IR (film): 3012, 2923, 2853, 1697, 1597, 1440, 1381, 1257, 1030, 836, 756 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.22 (d, 2H, *J* 5.9 Hz), 6.99 (dt, 2H, *J* 8.5, 2.1 Hz), 6.92 (brs, 1H), 6.71 (s, 2H), 6.13 (s, 1H), 4.07 (brs, 1H), 3.87 (s, 3H), 3.77 (d, 1H, *J* 15.1 Hz), 2.24 (s, 6H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.1, 161.8, 155.6, 139.5, 135.8, 130.2, 129.6, 123.0, 117.5, 114.7, 114.4, 55.4, 54.8, 33.9, 21.1. ESI-MS: *m/z* 398 (M+H)<sup>+</sup>. HRMS (ESI): *m/z* [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>20</sub>N<sub>3</sub>O<sub>4</sub>S: 398.1169; Found: 398.1169.

**3-[3-(3,4-Dimethylphenyl)-4-oxothiazolidin-2-yl]-4-(4-methoxyphenyl)-1,2,5-oxadiazole 2-oxide (8f).** White solid (78%), m.p. 120-122 °C, IR (film): 3012, 2056, 1697, 1597, 1137, 836, 593 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.24 (d, 2H, *J* 7.7 Hz), 7.10 (d, 1H, *J* 7.7 Hz), 7.02-6.96 (m, 2H), 6.85 (m, 2H), 6.13 (s, 1H), 4.05 (brd, 1H, *J* 15.1 Hz), 3.87 (s, 3H), 3.76 (d, 1H, *J* 15.1 Hz), 2.21 (s, 3H), 2.18 (s, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.2, 161.8, 155.6, 138.3, 137.3, 133.6, 130.7, 129.6, 126.5, 122.6, 117.5, 114.7, 114.5, 55.4, 54.8, 33.8, 19.7, 19.4. ESI-MS: *m/z* 398 (M+H)<sup>+</sup>. HRMS (ESI): *m/z* [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>20</sub>N<sub>3</sub>O<sub>4</sub>S: 398.1165; Found: 398.1162.

**4-(4-Methoxyphenyl)-3-[3-(4-methoxyphenyl)-4-oxothiazolidin-2-yl]-1,2,5-oxadiazole 2-oxide (8g).** White solid (78%), m.p. 112-114 °C, IR (film): 3009, 2936, 2840, 1695, 1590, 1448, 1025, 839, 745 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.21 (d, 2H, *J* 8.8 Hz), 7.04 (d, 2H, *J* 8.6 Hz), 6.98 (d, 2H, *J* 8.6 Hz), 6.86 (d, 2H, *J* 8.8 Hz), 6.08 (s, 1H), 4.06 (brd, 1H, *J* 14.9 Hz), 3.86 (s, 3H), 3.77 (s, 3H), 3.76 (d, 1H, *J* 14.9 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.4, 161.8, 159.4, 155.5, 129.5, 128.5, 127.1, 117.3, 115.0, 114.8, 114.4, 55.4, 54.9, 33.7. ESI-MS: *m/z* 400 (M+H)<sup>+</sup>. HRMS (ESI): *m/z* [M + H]<sup>+</sup> Calcd for C<sub>19</sub>H<sub>18</sub>N<sub>3</sub>O<sub>5</sub>S: 400.09617; Found: 400.0961.

**3-[3-(3,4-Dimethoxyphenyl)-4-oxothiazolidin-2-yl]-4-(4-methoxyphenyl)-1,2,5-oxadiazole 2-oxide (8h).** White solid (78%), m.p. 128-130 °C, IR (film): 3422, 2852, 1593, 1387, 1019, 692, 516 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.23 (d, 2H, *J* 8.6 Hz), 6.98 (d, 2H, *J* 8.6 Hz), 6.80 (d, 1H, *J* 8.4 Hz), 6.65 (dd, 2H, *J* 8.4, 2.2 Hz), 6.12 (s, 1H), 4.15-3.98 (m, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.82-3.73 (m, 4H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.3, 161.8, 155.5, 149.5, 148.9, 129.4, 128.6, 118.0, 117.3, 114.7, 114.4, 111.3, 108.8, 55.9, 55.8, 55.4, 54.9, 33.7. ESI-MS: *m/z* 430 (M+H)<sup>+</sup>. HRMS (ESI): *m/z* [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>20</sub>N<sub>3</sub>O<sub>6</sub>S: 430.1059; Found: 430.1061.

**3-[3-(1,3-Benzodioxol-5-yl)-4-oxothiazolidin-2-yl]-4-(4-methoxyphenyl)-1,2,5-oxadiazole 2-oxide (8i).** Brown solid (76%), m.p. 165-168 °C, IR (film): 3012, 2921, 2851, 1694, 1599, 1470, 1385, 1216, 837, 758 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.25 (brd, 2H, *J* 8.3 Hz), 7.03-6.98 (m, 2H), 6.76 (d, 1H, *J* 8.3 Hz), 6.64 (d, 1H, *J* 2.2 Hz), 6.58 (dd, 1H, *J* 8.3, 2.2 Hz), 6.05 (s, 1H), 5.98 (s, 2H), 4.06 (brd, 1H, *J* 15.1 Hz), 3.87 (s, 3H), 3.75 (d, 1H, *J* 15.1 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.4, 161.9, 155.5, 148.5, 147.7, 129.6, 129.5, 119.4, 117.3, 114.8, 114.3, 108.6, 107.2,

101.9, 55.4, 55.0, 33.7. ESI-MS:  $m/z$  414  $[M+H]^+$ . HRMS (ESI):  $m/z$   $[M + H]^+$  Calcd for  $C_{19}H_{16}N_3O_6S$ : 414.0754; Found: 414.0752.

**3-[3-(3-Fluorophenyl)-4-oxothiazolidin-2-yl]-4-(4-methoxyphenyl)-1,2,5-oxadiazole 2-oxide (8j)**. Brown solid (74%), m.p. 120-122 °C, IR (film): 2925, 2985, 1694, 1598, 1258, 1012, 760, 598  $cm^{-1}$ .  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  7.33-7.27 (m, 3H), 7.03-6.97 (m, 3H), 6.95-6.89 (m, 2H), 6.20 (s, 1H), 4.03 (brd, 1H,  $J$  15.1 Hz), 3.87 (s, 3H), 3.77 (d, 1H,  $J$  15.1 Hz).  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  170.0, 162.8 (d,  $J$  248.8 Hz), 161.8, 155.4, 137.5 (d,  $J$  9.9 Hz), 130.8 (d,  $J$  9.1 Hz), 129.5, 120.2, 117.2, 115.3 (d,  $J$  21.8 Hz), 114.9, 114.4, 112.7 (d,  $J$  23.6 Hz), 55.4, 54.4, 33.7. ESI-MS:  $m/z$  388  $(M+H)^+$ . HRMS (ESI):  $m/z$   $[M + H]^+$  Calcd for  $C_{18}H_{15}FN_3O_4S$ : 388.0761; Found: 388.0767.

**3-[3-(4-Fluorophenyl)-4-oxothiazolidin-2-yl]-4-(4-methoxyphenyl)-1,2,5-oxadiazole 2-oxide (8k)**. White solid (74%), m.p. 110-112 °C, IR (film): 3017, 2970, 2939, 1694, 1598, 1440, 1219, 1031, 837, 768  $cm^{-1}$ .  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  7.24 (brd, 2H,  $J$  8.6 Hz), 7.13-7.09 (m, 2H), 7.06-7.02 (m, 2H), 7.00 (d, 2H,  $J$  8.6 Hz), 6.13 (s, 1H), 4.06 (brd, 1H,  $J$  15.2 Hz), 3.87 (s, 3H), 3.77 (d, 1H,  $J$  15.2 Hz).  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  170.4, 161.9 (d,  $J$  250.2 Hz), 160.2, 155.5, 132.0 (d,  $J$  4.4 Hz), 129.5, 127.6 (d,  $J$  8.8 Hz), 117.2, 116.9 (d,  $J$  21.9 Hz), 114.9, 114.3, 55.5, 54.7, 33.7. ESI-MS:  $m/z$  388  $(M+H)^+$ . HRMS (ESI):  $m/z$   $[M + H]^+$  Calcd for  $C_{18}H_{15}FN_3O_4S$ : 388.0761; Found: 388.0767.

**3-[3-(3-Chlorophenyl)-4-oxothiazolidin-2-yl]-4-(4-methoxyphenyl)-1,2,5-oxadiazole 2-oxide (8l)**. Brown solid (76%), m.p. 125-128 °C, IR (film): 2983, 2937, 2840, 1703, 1602, 1456, 1259, 840, 786  $cm^{-1}$ .  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  7.31-7.24 (m, 4H), 7.13-7.11 (m, 1H), 7.05-7.00 (m, 3H), 6.18 (s, 1H), 4.05 (brd, 1H,  $J$  15.8 Hz), 3.88 (s, 3H), 3.77 (d, 1H,  $J$  15.8 Hz).  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  170.1, 162.0, 155.5, 137.2, 135.2, 130.6, 129.6, 128.4, 125.5, 123.0, 117.1, 114.9, 114.3, 55.5, 54.4, 33.8. ESI-MS:  $m/z$  404  $[M+H]^+$ . HRMS (ESI):  $m/z$   $[M + H]^+$  Calcd for  $C_{18}H_{15}^{35}ClN_3O_4S$ : 404.0466; Found: 404.0470; Calcd for  $C_{18}H_{15}^{37}ClN_3O_4S$ : 406.0437; Found: 406.0434.

**3-[3-(4-Chlorophenyl)-4-oxothiazolidin-2-yl]-4-(4-methoxyphenyl)-1,2,5-oxadiazole 2-oxide (8m)**. Brown solid (77%), m.p. 123-125 °C, IR (film): 3088, 2933, 2836, 1697, 1595, 1446, 1252, 836, 788  $cm^{-1}$ .  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  7.34-7.28 (m, 4H), 7.08 (d, 2H,  $J$  8.6 Hz), 7.02 (d, 2H,  $J$  8.6 Hz), 6.18 (s, 1H), 4.04 (brd, 1H,  $J$  15.2 Hz), 3.88 (s, 3H), 3.78 (d, 1H,  $J$  15.2 Hz).  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  170.1, 162.0, 155.4, 134.6, 134.0, 129.8, 129.5, 126.4, 117.2, 114.9, 114.3, 55.5, 54.5, 33.7. ESI-MS:  $m/z$  404  $[M+H]^+$ . HRMS (ESI):  $m/z$   $[M + H]^+$  Calcd for  $C_{18}H_{15}^{35}ClN_3O_4S$ : 404.0466; Found: 404.0469; Calcd for  $C_{18}H_{15}^{37}ClN_3O_4S$ : 406.0437; Found: 406.0435.

**3-[3-(4-Bromophenyl)-4-oxothiazolidin-2-yl]-4-(4-methoxyphenyl)-1,2,5-oxadiazole 2-oxide (8n)**. White solid (70%), m.p. 122-124 °C, IR (film): 3414, 2853, 1817, 1482, 1121, 759  $cm^{-1}$ .  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  7.47 (d, 2H,  $J$  8.6 Hz), 7.28 (d, 2H,  $J$  8.6 Hz), 7.04-7.00 (m, 4H), 6.18 (s, 1H), 4.03 (brd, 1H,  $J$  15.4 Hz), 3.88 (s, 3H), 3.77 (d, 1H, 15.4 Hz).  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  170.1, 162.0, 155.4, 135.1, 132.8, 129.5, 126.6, 122.0, 117.2, 114.9, 114.3, 55.5, 54.4, 33.7. ESI-

MS:  $m/z$  448 (M+H)<sup>+</sup>. HRMS (ESI):  $m/z$  [M+H]<sup>+</sup> Calcd for C<sub>18</sub>H<sub>15</sub><sup>79</sup>BrN<sub>3</sub>O<sub>4</sub>S: 447.9992; Found: 447.9992; Calcd for C<sub>18</sub>H<sub>15</sub><sup>81</sup>BrN<sub>3</sub>O<sub>4</sub>S: 449.9941; Found: 449.9948.

**4-[4-Fluorophenyl]-3-(4-oxo-3-phenylthiazolidin-2-yl)-1,2,5-oxadiazole 2-oxide (9a).** White solid (82%), m.p. 108-110 °C, IR (film): 3054, 2930, 2851, 1682, 1594, 1447, 1220, 840, 750, 696 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.39-7.35 (m, 2H), 7.33-7.29 (m, 1H), 7.28-7.24 (m, 2H), 7.21-7.17 (m, 2H), 7.13-7.10 (m, 2H), 6.14 (s, 1H), 4.04 (brd, 1H, *J* 15.4 Hz), 3.79 (d, 1H, *J* 15.4 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.1, 164.5 (d, *J* 252.5 Hz), 154.9, 136.0, 130.3 (d, *J* 8.8 Hz), 129.9, 128.6, 125.5, 121.4 (d, *J* 4.4 Hz), 116.8 (d, *J* 21.9 Hz), 114.3, 54.7, 33.8. ESI-MS:  $m/z$  358 [M+H]<sup>+</sup>. HRMS (ESI):  $m/z$  [M + H]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>13</sub>FN<sub>3</sub>O<sub>3</sub>S: 358.0656; Found: 358.0659.

**3-[3-(4-Butylphenyl)-4-oxothiazolidin-2-yl]-4-(4-fluorophenyl)-1,2,5-oxadiazole 2-oxide (9b).** White solid (78%), m.p. 90-93 °C, IR (film): 2926, 1692, 1597, 1216, 1039, 768 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.27-7.13 (m, 6H), 7.00 (d, 2H, *J* 8.3 Hz), 6.09 (s, 1H), 4.03 (d, 1H, *J* 15.2 Hz), 3.77 (d, 1H, *J* 15.2 Hz), 2.57 (t, 2H, *J* 7.7 Hz), 1.60-1.50 (m, 2H), 1.38-1.25 (m, 2H), 0.90 (t, 3H, *J* 7.7 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.2, 164.4 (d, *J* 252.5 Hz), 155.0, 143.8, 133.5, 130.3 (d, *J* 8.8 Hz), 129.8, 125.4, 121.4, 116.7 (d, *J* 21.9 Hz), 114.3, 54.8, 35.2, 33.8, 33.3, 22.2, 13.9. ESI-MS:  $m/z$  414 (M+H)<sup>+</sup>. HRMS (ESI):  $m/z$  [M+H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>21</sub>FN<sub>3</sub>O<sub>3</sub>S: 414.1282; Found: 414.1274.

**4-(4-Fluorophenyl)-3-[3-(4-isopropylphenyl)-4-oxothiazolidin-2-yl]-1,2,5-oxadiazole 2-oxide (9c).** White solid (78%), m.p. 160-161 °C, IR (film): 3416, 2961, 1599, 1444, 1186, 842 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.24-7.19 (m, 4H), 7.18-7.13 (m, 2H), 7.02 (d, 2H, *J* 8.5 Hz), 6.09 (s, 1H), 4.03 (brd, 1H, *J* 15.1 Hz), 3.76 (d, 1H, *J* 15.1 Hz), 2.88 (sept, 1H, *J* 7.0 Hz), 1.21 (d, 6H, *J* 7.0 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.0, 164.3 (d, *J* 253.4 Hz), 154.9, 149.5, 133.4, 130.2 (d, *J* 9.1 Hz), 127.8, 125.3, 121.3 (d, *J* 2.7 Hz), 116.5 (d, *J* 21.8 Hz), 114.2, 54.7, 33.6, 29.5, 23.7, 23.6. ESI-MS:  $m/z$  400 (M+H)<sup>+</sup>. HRMS (ESI):  $m/z$  [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>19</sub>FN<sub>3</sub>O<sub>3</sub>S: 400.1131; Found: 400.1116.

**3-[3-(4-*tert*-Butylphenyl)-4-oxothiazolidin-2-yl]-4-(4-fluorophenyl)-1,2,5-oxadiazole 2-oxide (9d).** White solid (76%), m.p. 175-178 °C, IR (film): 2992, 2965, 2934, 1696, 1589, 1384, 1222, 1020, 842, 782, 623 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.38 (d, 2H, *J* 8.6 Hz), 7.22-7.13 (m, 4H), 7.03 (d, 2H, *J* 8.6 Hz), 6.08 (s, 1H), 4.02 (brd, 1H, *J* 15.2 Hz), 3.77 (d, 1H, *J* 15.2 Hz), 1.28 (s, 9H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.1, 164.3 (d, *J* 253.4 Hz), 154.9, 151.8, 133.2, 130.3 (d, *J* 8.1 Hz), 126.8, 125.0, 121.4 (d, *J* 2.7 Hz), 116.6 (d, *J* 21.8 Hz), 114.3, 54.7, 34.6, 33.7, 31.1. ESI-MS:  $m/z$  414 (M+H)<sup>+</sup>. HRMS (ESI):  $m/z$  [M + H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>21</sub>FN<sub>3</sub>O<sub>3</sub>S: 414.1282; Found: 414.1276.

**3-[3-(3,5-Dimethylphenyl)-4-oxothiazolidin-2-yl]-4-(4-fluorophenyl)-1,2,5-oxadiazole 2-oxide (9e).** White solid (76%), m.p. 178-180 °C, IR (film): 2920, 2854, 1689, 1603, 1453, 1231, 1030, 839, 733, 622 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.30-7.17 (m, 4H), 6.93 (brs, 1H), 6.72 (s, 2H), 6.10 (s, 1H), 4.05-4.00 (m, 1H), 3.74 (d, 1H, *J* 15.2 Hz), 2.24 (s, 6H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 169.9, 164.4 (d, *J* 253.6 Hz), 154.9, 139.6, 135.8, 130.4 (d, *J* 8.8 Hz), 130.2, 123.0, 121.6 (d, *J* 2.7 Hz), 116.6 (d, *J* 22.0 Hz), 114.2, 54.7, 33.8, 21.1. ESI-MS:  $m/z$  386 (M+H)<sup>+</sup>. HRMS (ESI):  $m/z$  [M + H]<sup>+</sup> Calcd for C<sub>19</sub>H<sub>17</sub>FN<sub>3</sub>O<sub>3</sub>S: 386.0969; Found: 386.0967.

**3-[3-(3,4-Dimethylphenyl)-4-oxothiazolidin-2-yl]-4-(4-fluorophenyl)-1,2,5-oxadiazole 2-oxide (9f).** White solid (79%), m.p. 145-147 °C, IR (film): 3421, 1675, 1603, 1452, 839, 585 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.30-7.26 (m, 2H), 7.17 (dt, 2H, *J* 8.5, 1.8 Hz), 7.10 (d, 1H, *J* 7.9 Hz), 6.87-6.82 (m, 2H), 6.12 (s, 1H), 4.07-3.97 (m, 1H), 3.80-3.72 (m, 1H), 2.21 (s, 3H), 2.17 (s, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 169.8, 164.1 (d, *J* 253.6 Hz), 154.8, 138.2, 137.2, 133.5, 130.6, 130.2 (d, *J* 8.8 Hz), 126.3, 122.5, 121.4 (d, *J* 2.7 Hz), 116.5 (d, *J* 22.0 Hz), 114.2, 54.6, 33.6, 19.5, 19.2. ESI-MS: *m/z* 386 (M+H)<sup>+</sup>. HRMS (ESI): *m/z* [M + H]<sup>+</sup> Calcd for C<sub>19</sub>H<sub>17</sub>FN<sub>3</sub>O<sub>3</sub>S: 386.0896; Found: 386.0963.

**4-(4-Fluorophenyl)-3-[3-(4-methoxyphenyl)-4-oxothiazolidin-2-yl]-1,2,5-oxadiazole 2-oxide (9g).** White solid (77%), m.p. 142-144 °C, IR (film): 3005, 2934, 2842, 1683, 1592, 1440, 1228, 836, 817, 773 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.31-7.24 (m, 2H), 7.22-7.14 (m, 2H), 7.03 (d, 2H, *J* 9.0 Hz), 6.87 (d, 2H, *J* 9.0 Hz), 6.05 (s, 1H), 4.05 (brd, 1H, *J* 15.2 Hz), 3.78 (s, 3H), 3.77 (d, 1H, *J* 15.2 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.2, 164.4 (d, *J* 252.5 Hz), 159.4, 154.8, 130.3 (d, *J* 8.8 Hz), 128.4, 127.1, 121.4, 116.8 (d, *J* 21.9 Hz), 115.0, 114.2, 55.4, 54.8, 33.6. ESI-MS: *m/z* 388 (M+H)<sup>+</sup>. HRMS (ESI): *m/z* [M + H]<sup>+</sup> Calcd for C<sub>18</sub>H<sub>15</sub>FN<sub>3</sub>O<sub>4</sub>S: 388.0761; Found: 388.0758.

**3-[3-(3,4-Dimethoxyphenyl)-4-oxothiazolidin-2-yl]-4-(4-fluorophenyl)-1,2,5-oxadiazole 2-oxide (9h).** White solid (77%), m.p. 160-163 °C, IR (film): 3353, 2966, 2044, 1684, 1445, 1099 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.33-7.26 (m, 2H), 7.23-7.15 (m, 2H), 6.81 (d, 1H, *J* 8.4 Hz), 6.67 (dd, 1H, *J* 8.4, 2.4 Hz), 6.62 (d, 1H, *J* 2.4 Hz), 6.08 (s, 1H), 4.06 (brd, 1H, *J* 15.4 Hz), 3.86 (s, 3H), 3.79 (d, 1H, *J* 15.4 Hz), 3.76 (s, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.2, 164.4 (d, *J* 253.4 Hz), 154.9, 149.6, 149.0, 130.2 (d, *J* 8.2 Hz), 128.6, 121.4 (d, *J* 1.8 Hz), 117.9, 116.7 (d, *J* 22.7 Hz), 114.2, 111.3, 108.8, 55.9, 55.9, 54.8, 33.6. ESI-MS: *m/z* 418 [M+H]<sup>+</sup>. HRMS (ESI): *m/z* [M + H]<sup>+</sup> Calcd for C<sub>19</sub>H<sub>17</sub>FN<sub>3</sub>O<sub>5</sub>S: 418.0858; Found: 418.0860.

**3-[3-(1,3-Benzodioxol-5-yl)-4-oxothiazolidin-2-yl]-4-(4-fluorophenyl)-1,2,5-oxadiazole 2-oxide (9i).** White solid (74%), m.p. 180-182 °C, IR (film): 3069, 2908, 1681, 1587, 1444, 1038, 845, 777, 628, 669 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.35-7.29 (m, 2H), 7.25-7.18 (m, 2H), 6.77 (d, 1H, *J* 8.3 Hz), 6.63 (d, 1H, *J* 2.2 Hz), 6.57 (dd, 1H, *J* 8.3, 2.2 Hz), 6.01 (s, 1H), 5.99 (s, 2H), 4.06 (brd, 1H, *J* 15.8 Hz), 3.77 (d, 1H, *J* 15.8 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.4, 163.8 (d, *J* 251.3 Hz), 148.6, 141.7, 140.8, 130.3 (d, *J* 8.8 Hz), 129.5, 119.5, 116.9 (d, *J* 21.9 Hz), 114.2, 108.8, 107.2, 102.0, 94.8, 54.9, 33.7. ESI-MS: *m/z* 402 [M+H]<sup>+</sup>. HRMS (ESI): *m/z* [M + H]<sup>+</sup> Calcd for C<sub>18</sub>H<sub>13</sub>FN<sub>3</sub>O<sub>5</sub>S: 402.0554; Found: 402.0546.

**4-(4-Fluorophenyl)-3-[3-(3-fluorophenyl)-4-oxothiazolidin-2-yl]-1,2,5-oxadiazole 2-oxide (9j).** White solid (73%), m.p. 128-131 °C, IR (film): 2928, 1680, 1387, 622, 567 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.36-7.30 (m, 3H), 7.25-7.21 (m, 2H), 7.03-6.99 (m, 1H), 6.93-6.89 (m, 2H), 6.17 (s, 1H), 4.01 (brd, 1H, *J* 15.4 Hz), 3.80 (d, 1H, *J* 15.4 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.0, 165.0 (d, *J* 254.4 Hz), 162.9 (d, *J* 247.9 Hz), 164.5, 130.9 (d, *J* 8.8 Hz), 130.3 (d, *J* 8.8 Hz), 120.3 (d, *J* 4.4 Hz), 117.0 (d, *J* 21.9 Hz), 116.9, 115.8 (d, *J* 21.9 Hz), 115.4, 114.3, 112.7 (d, *J* 24.1 Hz), 54.4, 33.8. ESI-MS: *m/z* 376 [M+H]<sup>+</sup>. HRMS (ESI): *m/z* [M + H]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>12</sub>F<sub>2</sub>N<sub>3</sub>O<sub>3</sub>S: 376.0561; Found: 376.0566.

**4-(4-Fluorophenyl)-3-[3-(4-fluorophenyl)-4-oxothiazolidin-2-yl]-1,2,5-oxadiazole 2-oxide (9k).** White solid (74%), m.p. 148-150 °C, IR (film): 3075, 2927, 2852, 1681, 1595, 1508, 1387, 1217, 843, 776, 619, 588 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.34-7.28 (m, 2H), 7.24-7.19 (m, 2H), 7.13-7.08 (m, 2H), 7.08-7.02 (m, 2H), 6.11 (s, 1H), 4.05 (brd, 1H, *J* 15.2 Hz), 3.79 (d, 1H, *J* 15.2 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.3, 164.6 (d, *J* 254.7 Hz), 162.0 (d, *J* 248.1 Hz), 154.8, 131.9 (d, *J* 4.4 Hz), 130.7 (d, *J* 8.8 Hz), 127.5 (d, *J* 6.6 Hz), 121.3, 117.0 (d, *J* 21.9 Hz), 116.8 (d, *J* 21.9 Hz), 114.1, 54.7, 33.6. ESI-MS: *m/z* 376 (M+H)<sup>+</sup>. HRMS (ESI): *m/z* [M + H]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>12</sub>F<sub>2</sub>N<sub>3</sub>O<sub>3</sub>S: 376.0561; Found: 376.0564.

**3-[3-(3-Chlorophenyl)-4-oxothiazolidin-2-yl]-4-(4-fluorophenyl)-1,2,5-oxadiazole 2-oxide (9l).** White solid (74%), m.p. 105-107 °C, IR (film): 3001, 2929, 1599, 1444, 850, 618 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.35-7.31 (m, 2H), 7.29-7.26 (m, 2H), 7.24-7.20 (m, 2H), 7.11-7.10 (m, 1H), 7.04-7.01 (m, 1H), 6.17 (s, 1H), 4.03 (brd, 1H, *J* 15.4 Hz), 3.78 (d, 1H, *J* 15.4 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.0, 166.2 (d, *J* 252.4 Hz), 154.8, 137.1, 135.3, 130.7, 130.4 (d, *J* 8.8 Hz), 128.6, 125.4, 123.0, 121.2, 116.9 (d, *J* 21.9 Hz), 114.2, 54.4, 33.7. ESI-MS: *m/z* 392 (M+H)<sup>+</sup>. HRMS (ESI): *m/z* [M + H]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>12</sub>F<sup>35</sup>ClN<sub>3</sub>O<sub>3</sub>S: 392.0266; Found: 392.0269; Calcd for C<sub>17</sub>H<sub>12</sub>F<sup>37</sup>ClN<sub>3</sub>O<sub>3</sub>S: 394.0237; Found: 394.0234.

**3-[3-(4-Chlorophenyl)-4-oxothiazolidin-2-yl]-4-(4-fluorophenyl)-1,2,5-oxadiazole 2-oxide (9m).** White solid (82%), m.p. 109-110 °C, IR (film): 2974, 2929, 2851, 1686, 1601, 1445, 1384, 1217, 842, 786, 620 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.36-7.31 (m, 4H), 7.25-7.20 (m, 2H), 7.08-7.05 (m, 2H), 6.15 (s, 1H), 4.01 (d, 1H, *J* 15.4 Hz), 3.79 (d, 1H, *J* 15.4 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 170.0, 164.4 (d, *J* 254.68 Hz), 154.7, 134.3 (d, *J* 21.9 Hz), 130.3 (d, *J* 8.8 Hz), 130.0, 129.0, 126.4, 121.3, 116.9 (d, *J* 21.9 Hz), 114.2, 54.4, 33.7. ESI-MS: *m/z* 392 [M+H]<sup>+</sup>. HRMS (ESI): *m/z* [M + H]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>12</sub>F<sup>35</sup>ClN<sub>3</sub>O<sub>3</sub>S: 392.0266; Found: 392.0269. Calcd for C<sub>17</sub>H<sub>12</sub>F<sup>37</sup>ClN<sub>3</sub>O<sub>3</sub>S: 394.0237; Found: 394.0235.

**3-[3-(4-Bromophenyl)-4-oxothiazolidin-2-yl]-4-(4-fluorophenyl)-1,2,5-oxadiazole 2-oxide (9n).** Brown solid (70%), m.p. 147-150 °C, IR (film): 3356, 2929, 1686, 1443, 1287, 1162, 587 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.48 (d, 2H, *J* 8.6 Hz), 7.38-7.32 (m, 2H), 7.26-7.19 (m, 2H), 7.01 (d, 2H, *J* 8.6 Hz), 6.16 (s, 1H), 4.01 (d, 1H, *J* 15.4 Hz), 3.79 (d, 1H, *J* 15.4 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 169.9, 164.1 (d, *J* 254.7 Hz), 154.8, 134.9, 132.9, 130.3 (d, *J* 8.7 Hz), 126.6, 122.1, 121.3, 116.9 (d, *J* 21.9 Hz), 114.3, 54.3, 33.6. ESI-MS: *m/z* 459 [M+Na]<sup>+</sup>. HRMS (ESI): *m/z* [M + Na]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>11</sub>F<sup>79</sup>BrN<sub>3</sub>O<sub>3</sub>SNa: 457.9581; Found: 457.9585; Calcd for C<sub>17</sub>H<sub>11</sub>F<sup>81</sup>BrN<sub>3</sub>O<sub>3</sub>SNa: 459.9561; Found: 459.9555.

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