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Selective Synthesis of *Ortho*-Substituted 2-Aryl-3-Phenyl-1,3-Thiazolidin-4-one Sulfoxides and Sulfones by *S*-Oxidation with Oxone®

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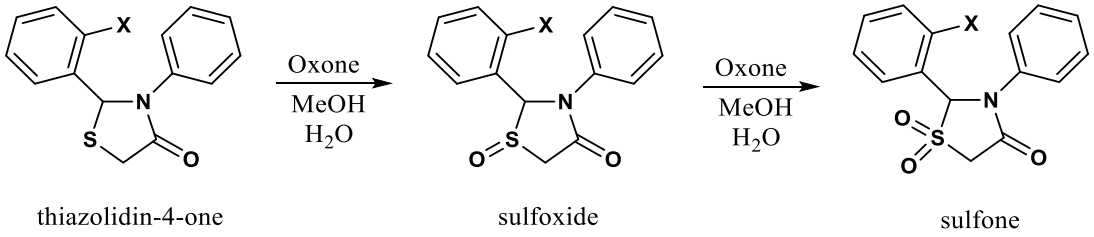
Abstract

S-oxidation of 2-aryl-3-phenyl-1,3-thiazolidin-4-ones with Oxone® was investigated. For all compounds evaluated, selective oxidation to the sulfoxide was realized using 3 equivalents of Oxone® at room temperature. Attempts to selectively prepare the sulfones of *ortho*-substituted 2-aryl-3-phenyl-1,3-thiazolidin-4-ones at high temperature by increasing the equivalents of Oxone® used were typically unsuccessful. These results contrast significantly with *ortho*-substituted 2-aryl-3-cyclohexyl-1,3-thiazolidin-4-ones evaluated previously. The extent of this selectivity was affected by the substituent and its position on the C2 aromatic ring. The ratio of the sulfoxide and sulfone products was quantified by isolating the products by liquid chromatography.



Keywords: thiazolidin-4-ones, Oxone, sulfoxide, sulfone

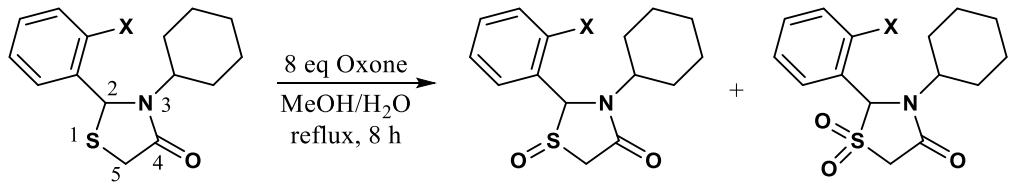
1. Introduction

1,3-Thiazolidin-4-ones, also known as thiazolidin-4-ones, are known to have a very wide range of biological activity.(Suryawanshi et al., 2017)(Kaushal & Kaur, 2016)(Kumar, Kumar, Mundlia, Pradhan & Malik, 2015)(Tripathi et al., 2014)(Jain, Vaidya, Ravichandran, Kashaw, & Agrawal, 2012)(Abhinit, Ghodke & Pratima, 2009)(Hamama, Ismail, Shaaban & Zoorob, 2008)(Singh, Parmar, Raman, Virgil & Stenberg, 1981)(Brown, 1961), so much that some have referred to it as a "magic moiety" or "wonder nucleus"(Jain et al., 2012). The *S*-oxides may show enhanced activity; for example, Miller and coworkers converted one 4-thiazolidinone to its sulfoxide and sulfone and reported that the oxides showed greater activity against some cancer cell lines than the sulfide.(Gududuru, Hurh, Dalton & Miller, 2004) Thiazolidin-4-ones have been oxidized to sulfoxides with peracetic acid (Surrey, 1967), Na_5IO_6 (Smith, Lee & Cragoe, 1977), chloramine T (Omar, El-Kharmy & Sharif, 1981), $NaIO_4$ (Lee, Yergatian, Crowther & Downie, 1990), Oxone® (one example)(Rozwadowska, Sulima & Gzella, 2002), and *m*-CPBA (Rozwadowska & Sulima, 2003). Oxidation from sulfide to sulfoxide makes the sulfur a chiral center, and produces *cis* and *trans* diastereomers with relation to C-2 (Rozwadowska et al., 2002) (Colombo et al., 2008). The stereocenters, however, may be configurationally unstable (Rozwadowska et al., 2002). Oxidation of thiazolidin-4-ones to sulfones has been accomplished with H_2O_2/Ac_2O/AcOH (Troutman & Long, 1948), and $KMnO_4$ (Surrey, 1948).

Oxone®, a mixture of potassium sulfates (2 $KHSO_5$/1 K_2SO_4/1 $KHSO_4$), is a very desirable material to use because it is a "green" reagent which is inexpensive, safe, and easy to use (Yu et al., 2012) (Hussain, Green & Ahmed, 2013). It has been

used as a chemoselective reagent for the oxidation of sulfides to either sulfoxides (Trost & Curran, 1981) (Yu et al., 2012) (Webb, 1994) (Madesclaire, 1986) or sulfones (Trost & Curran, 1981) (Yu et al., 2012) (Webb, 1994). Selectivity toward the sulfoxide or sulfone has been shown to depend on the amount of Oxone® used, the temperature, and the solvent (Trost & Curran, 1981) (Yu et al., 2012) (Webb, 1994).

Although there are ample examples of Oxone®-based oxidations of sulfides, there is little data related specifically to the oxidation of thiazolidin-4-ones. Rozwadowska et al., (2002) reported a single example of oxidation of a thiazolidin-4-one to its sulfoxide with this reagent. Convenient synthetic access to thiazolidin-4-one *S*-oxides would encourage further biological and pharmaceutical evaluation of these compounds, which prompted our current investigation. We have previously reported the reaction of *ortho*-substituted 2-aryl-3-cyclohexyl-1,3-thiazolidin-4-ones with Oxone® (Cannon et al., 2015). For all ten compounds previously evaluated, selective oxidation to the sulfoxide was realized using 3 equivalents of Oxone® at room temperature, and subsequent oxidation to the sulfone was not observed under these reaction conditions after 25 hours. Alternatively, the sulfones were prepared with variable selectively at higher temperature (refluxing aqueous methanol) by increasing the equivalents of Oxone® used to 8.(Scheme 1) The extent of this selectivity was affected by the substituent on the C2 aromatic ring; sulfones were produced exclusively when the substituent (X) was OCH_3, OCH_2CH_3, or NO_2. Sulfone formation was significantly favored when the substituent was CH_3 or H. Slight preference for sulfone versus sulfoxide formation was observed when the substituent (X) was CF_3, but preference for sulfoxide formation was observed for halide substituents (X = F or Br). No clear pattern of reactivity was realized based on the substituents' electronic properties or size.



X = H, F, Cl, Br, CH_3, CF_3, OCH_3, OCH_2CH_3, NO_2, 1-naphthyl

Scheme 1. Oxidation of thiazolidin-4-ones using high temperature Oxone®-based reaction conditions

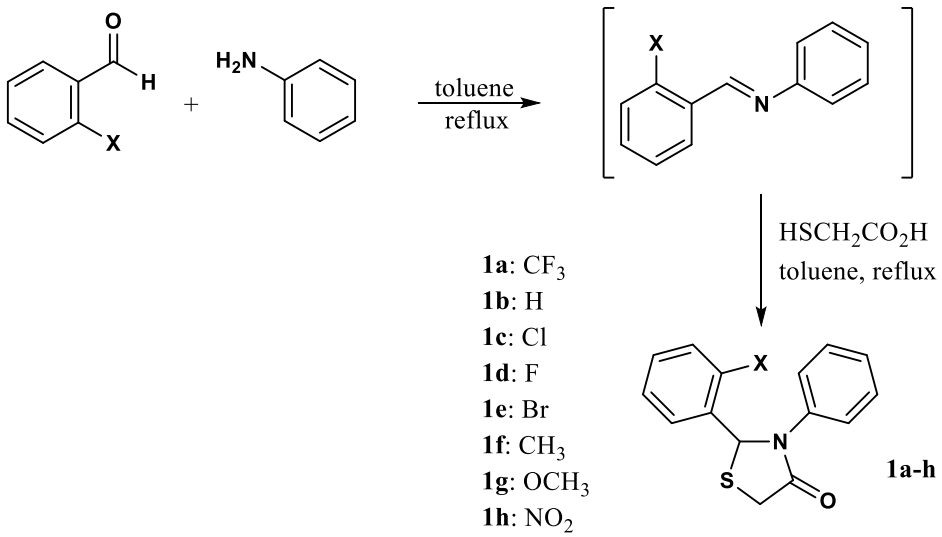
A subsequent evaluation of *S*-oxidation of *meta*- and *para*-substituted 3-aryl-2-phenyl-1,3-thiazolidin-4-ones with Oxone® likewise demonstrated selective oxidation to the sulfoxide using 3 equivalents of Oxone® at room temperature (Cannon, et al., 2017). At high temperature oxidations using 8 equivalents of Oxone®, the extent of selectivity in sulfone formation was affected by the substituent and its location on the N3 aromatic ring. The only clear substituent/reactivity correlation evidenced was better selectivity of sulfone versus sulfoxide formation when electron donating substituents (X = CH_3 and OCH_3) were in the *para* position; for all other substituents, *meta* substitution showed higher sulfone selectivity versus *para* substitution. Unlike the *ortho*-substituted 2-aryl-3-cyclohexyl-1,3-thiazolidin-4-ones, exclusive formation of sulfone versus sulfoxide was never realized by Oxone® oxidation, and overall yields decreased significantly. Exclusive sulfone formation was best achieved using 2 equivalents of $KMnO_4$.

In this study, we report the high temperature oxidation of a series of *ortho*-substituted 2-aryl-3-phenyl-1,3-thiazolidin-4-ones with Oxone® to determine if changing the N3 substituent from cyclohexyl to phenyl affects oxidative selectivity. We also report room temperature oxidations of this series of thiazolidin-4-ones with Oxone® and $KMnO_4$ to ascertain the scope and selectivity of the Oxone® oxidations.

2. Results and Discussion

2.1 Preparation of Ortho-Substituted Thiazolidin-4-Ones

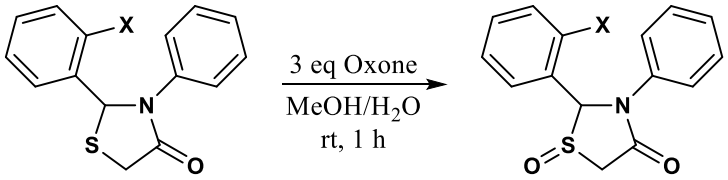
The *ortho*-substituted 2-aryl-3-phenyl-1,3-thiazolidin-4-ones **1a-h** used in this evaluation were prepared by sequential condensation reactions.(Tierney et al., 2005) The compounds were prepared by condensation of an *ortho*-substituted benzaldehyde with aniline to produce an imine intermediate, followed by condensation with thioglycolic acid (Scheme 2). Reaction progress in both steps was monitored by the collection of water in a Dean-Stark trap.



Scheme 2. Synthesis of *ortho*-substituted 3-aryl-2-phenyl-1,3-thiazolidin-4-ones **1a-h**

2.2 Low Temperature Oxone® Oxidations of Thiazolidin-4-Ones

Exclusive formation of sulfoxide compounds **2a-2h** was realized by performing the oxidation at room temperature with a 3 equivalents of Oxone® (Scheme 3). The reaction time for sulfoxide formation at 1h insured complete conversion of the thiazolidin-4-ones which was confirmed by thin layer chromatography (TLC). Results are summarized in Table 1. Clearly, low temperature oxidation with a reduced number of Oxone® equivalents favors sulfoxide formation as was previously observed for the 3-cyclohexyl-thiazolidin-4-ones (Cannon et al., 2015).



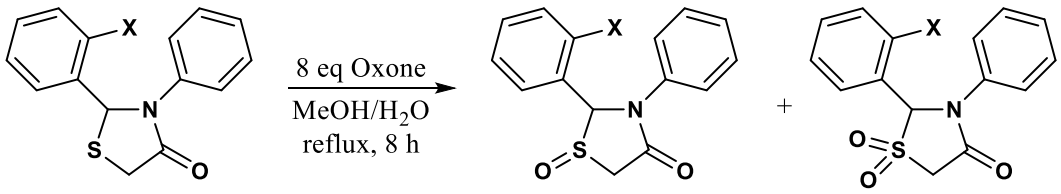
Scheme 3. Selective low temperature Oxone® oxidation of thiazolidin-4-ones to sulfoxides

Table 1. *Ortho*-substituted 2-aryl-3-phenyl-1,3-thiazolidin-4-one sulfoxides **2a-2h** synthesized according to Scheme 3

Product	% Yield	Melting Point (^oC)	R_f (3:1 cyclohexane:EtOAc)
2a, X = CF_3	98	oil	0.199
2b, X = H	96	163-164	0.159
2c, X = Cl	99	60-62	0.158
2d, X = F	99	179-180	0.098
2e, X = Br	83	154-155	0.135
2f, X = CH_3	99	172-174	0.154
2g, X = OCH_3	99	184-185	0.084
2h, X = NO_2	98	78-79	0.167

2.3 High Temperature Oxone® Oxidations of Thiazolidin-4-Ones

Compounds **1a-h** were oxidized according to the high temperature Oxone®-based reaction conditions that had been previously optimized for 2-aryl-3-cyclohexyl-1,3-thiazolidin-4-ones (Cannon et al., 2015) to compare selective formation of sulfones between the two sets of thiazolidin-4-ones (Scheme 4). Results are presented in Table 2.



1a-h **2a-h** **3a-h**

Scheme 4. High temperature Oxone® oxidation of *ortho*-substituted thiazolidin-4-ones

The ratio indicates the relative amounts of sulfoxide to sulfone isolated by chromatography. Also included are the ratios observed for the respective *ortho*-substituted 2-aryl-3-cyclohexyl-1,3-thiazolidin-4-ones. (Cannon et al., 2015)

Table 2. Oxidation of thiazolidin-4-ones **1a-h** using high temperature Oxone®-based reaction conditions

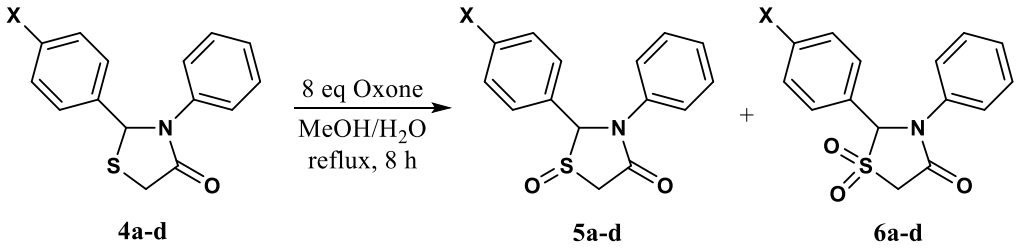
Thiazolidin-4-one (**1**)	Sulfoxide:Sulfone (**2**:**3**) (Total Yield)	Sulfoxide:Sulfone and Total Yield for the respective *N*-Cyclohexyl-substituted Thiazolidin-4-one
1a, X = CF_3	1.0:1.5 (89%)	1.0: 1.7 (89%)
1b, X = H	2.0:1.0 (76%)	1.0:3.2 (93%)
1c, X = Cl	1.1:1.0 (62%)	1.0:1.2 (98%)
1d, X = F	1.0:1.1 (66%)	2.0:1.0 (95%)
1e, X = Br	1.0:1.1 (62%)	2.1:1.0 (88%)
1f, X = CH_3	1.0:1.3 (80%)	1.0:4.9 (75%)
1g, X = OCH_3	1.1:1.0 (81%)	Sulfone only (98%)
1h, X = NO_2	7.6:1.0 (72%)	Sulfone only (94%)

Results in Table 2 show that sulfone formation significantly varied according to the substituent on N3. Only four of the eight *N*-phenyl-substituted thiazolidin-4-ones **1a**–**1h** demonstrated a preference for sulfone formation, and the highest preference was an anemic 20% excess observed for **1a** (X = CF_3). In contrast, the *N*-cyclohexyl-substituted thiazolidin-4-ones (Cannon, et al., 2015) demonstrated preferential sulfone formation for six of the eight compounds indicated, and exclusive sulfone formation was observed for both the corresponding methoxy and nitro derivatives. Even more interesting is that no substitution/reactivity correlations exist between the two sets of data. Preferences for sulfoxide versus sulfone formation flip for six of the eight aryl substituents, with the most significant changes in preference being observed for **1g** and **1h**. The corresponding *N*-cyclohexyl-substituted thiazolidin-4-ones previously had demonstrated exclusive sulfone formation, while **1g** and **1h** showed the third and first highest preference for sulfoxide formation, respectively, in the current evaluation.

Overall, the total oxidation yields are lower for the 2-aryl-3-phenyl-1,3-thiazolidin-4-ones (average yield = 74%) versus similarly substituted 2-aryl-3-cyclohexyl-1,3-thiazolidin-4-ones (average yield = 91%) despite reactant conversions of 100% for all thiazolidin-4-ones evaluated. In a prior publication, diaryl thiazolidin-4-one sulfones were stable under reaction conditions (8 Oxone® equivalents in refluxing aqueous methanol for 8 h) as determined by TLC and sulfone recovery (Cannon, et al., 2017). Therefore, product decomposition cannot account for either the lower observed oxidation yields or the relatively higher sulfoxide formation.

To further test the potential effect of C2 aryl substitution on sulfone formation and yields, a small group of *para*-substituted 2-aryl-3-phenyl-1,3-thiazolidin-4-ones (**4a**-**4d**) was evaluated under the same reaction conditions for high temperature oxidation (Scheme 5). The *para*-substituted and *ortho*-substituted thiazolidin-4-ones should have similar electronic properties, but the *para*-substituted thiazolidin-4-ones lack potential steric contributions associated with ortho substitution. Results summarized in Table 3 show better selectivity for sulfone formation and slightly improved oxidation yields for three of the four *para*-substituted thiazolidin-4-ones tested (**4a**, **4b**, and **4d**). Extensive decomposition of **4c** during the high temperature Oxone® oxidation accounted for the low yield of oxidation products. Attempts to characterize the aldehyde- and alkene-containing decomposition by-products of **4c** oxidation by NMR analysis were unsuccessful. Comparison of **1d** (X =

F), **1e** (X = Br), and **1h** (X = NO_2) to **4a**, **4b**, and **4d** show that the position of the substituent in the C2 aryl ring significantly changed sulfone formation selectivity, and that this effect is probably sterically based. Room temperature oxidations of **4a**-**4d** with Oxone® according to reaction conditions described previously produced the corresponding sulfoxides **5a**-**5d** exclusively as observed for **1a**-**1h**. Data for these products can be found in the experimental section.



4a-d **5a-d** **6a-d**

Scheme 5. High temperature Oxone® oxidation of *para*-substituted thiazolidin-4-ones

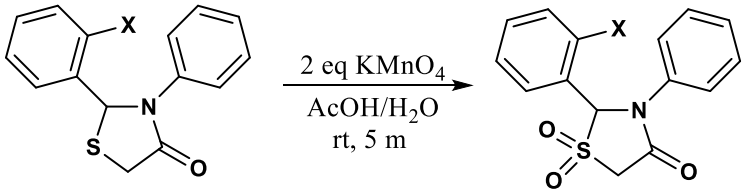
The ratio indicates the relative amounts of sulfoxide to sulfone isolated by chromatography.

Table 3. Oxidation of thiazolidin-4-ones **4a-d** using high temperature Oxone®-based reaction conditions

Thiazolidin-4-one (**4**)	Sulfoxide:Sulfone (**5**:**6**) (Total Yield)
4a, X = F	1.0:2.0 (79%)
4b, X = Br	1.0:1.8 (77%)
4c, X = OCH_3	1.0:1.0 (33%)
4d, X = NO_2	1.0:1.8 (82%)

2.4 $KMnO_4$-based Oxidations of Thiazolidin-4-Ones

Since Oxone® oxidations of 2-aryl-3-phenyl-1,3-thiazolidin-4-ones failed to produce sulfones with good selectivity, an alternative syntheses of the sulfones using aqueous $KMnO_4$ was evaluated (Surrey, 1948). This method was applied to compounds **1a**-**1h** to produce the corresponding sulfones (Scheme 6); results are summarized in Table 4. Although no measures were taken to optimize this reaction, the oxidation yields are overall significantly higher for the 2-aryl-3-phenyl-1,3-thiazolidin-4-ones (average yield=75%) compared to the 2-aryl-3-cyclohexyl-1,3-thiazolidin-4-ones (average yield = 56 %) previously synthesized by this method (Cannon et al., 2015).



1a-h **3a-h**

Scheme 6. $KMnO_4$ oxidation of thiazolidin-4-ones to sulfones

Table 3. *Ortho*-substituted 2-aryl-3-phenyl-1,3-thiazolidin-4-one sulfones **3a**-**h** synthesized according to Scheme 6

Product	% Yield	Melting Point (°C)
3a, X = CF_3	73	oil
3b, X = H	76	178-180
3c, X = Cl	69	oil
3d, X = F	76	159-160
3e, X = Br	91	oil
3f, X = CH_3	70	143-144
3g, X = OCH_3	80	130-131
34, X = NO_2	63	177-179

The $KMnO_4$ oxidation procedure was likewise applied to the *para*-substituted 2-aryl-3-phenyl-1,3-thiazolidin-4-ones **4a**-**4d** to produce the corresponding sulfones **6a**-**6d**. Data for these products can be found in the experimental section.

3. Conclusion

S-oxidation of 2-aryl-3-phenyl-1,3-thiazolidin-4-ones with Oxone® was dependent on the reaction temperature, equivalents of Oxone® used, the substituent, and the substituent's location on the C2 aromatic ring. For all thiazolidin-4-ones evaluated in this study, selective oxidation to the sulfoxide was realized by using 3 equivalents of Oxone® at room temperature. At high temperature using 8 equivalents of Oxone®, oxidative yields the selectivity in sulfone formation varied according to the substituent although no clear substituent/reactivity correlation was evident based on the substituents' electronic properties. Location of the substituent on the C2 aromatic ring appeared to be important as well: *para*-substituted C2 aryls demonstrated slightly better sulfone formation selectivity than *ortho*-substituted C2 aryls according to the limited number of *para*-substituted compounds evaluated. Substitution at N3 of the thiazolidin-4-one ring also affects sulfone selectivity and yield. Unlike the Oxone® oxidation of *ortho*-substituted 2-aryl-3-cyclohexyl-1,3-thiazolidin-4-ones evaluated previously, exclusive formation of sulfone versus sulfoxide was never realized for 2-aryl-3-phenyl-1,3-thiazolidin-4-ones, and in fact most sulfone selectivity was poor. Exclusive sulfone formation was best achieved using 2 equivalents of $KMnO_4$. Additionally, lower Oxone® oxidation yields were observed for *N*-phenyl thiazolidin-4-ones compared to previously evaluated *N*-cyclohexyl thiazolidin-4-ones.

4. Experimental

Reagent chemicals were obtained from commercial suppliers; Oxone® was purchased from Aldrich Chemical Company. TLC and chromatography plates (silica gel GF, 250 micron) were purchased from Analtech. Reagent grade solvents were used without further purification.

Most spectra were recorded on a Bruker 300 at 298K observing ^1H and ^{13}C at 300.15 and 75.48 MHz, respectively. These samples were dissolved in $CDCl_3$ at a concentration of 100 mg/mL using precision bore 5 mm NMR tubes supplied by Norell, Inc. The spectrometer was locked to either the deuterium or carbon resonance of $CDCl_3$ and all chemical shifts were referenced to residual $CHCl_3$.

Infrared spectra were obtained as an evaporated thin film on a sodium chloride plate (Janos Technology, Inc) on a Nicolet Nexus 670 spectrometer using 32 scans at a 2 cm^{-1} resolution. Mass spectra were recorded on a Varian 2100 G ion trap mass spectrometer, fitted with a Varian 3900 gas chromatograph: column - Factor 4 VF-5ms 0.25 mm id, 30 m, 0.25 μm film thickness, He carrier gas, 1.0 ml/min flow, 80 ℃ for 1 minute isothermal 15 ℃/min to 275 ℃ then 275 ℃ for 3 minutes isothermal, injector temp 250 ℃, 0 min, 1:50 split. Melting points are uncorrected; a Uni-Melt capillary melting point apparatus was used.

4.1 Preparation of Substituted-2-Aryl-3-Phenyl-Thiazolidin-4-Ones

All thiazolidine-4-ones were prepared using the procedure previously described. (Tierney et al., 2005) The *para*-substituted-2-aryl-3-phenyl-thiazolidin-4-ones **4a**-**4d** and **1b** had been previously characterized. (Tierney et al., 1996) Isolated yields of the *ortho*-substituted thiazolidine-4-ones **1a**-**1h** are based on aniline as the limiting reactant; no attempt was made to maximize the product yields. Thiazolidin-4-ones were purified by recrystallization using methanol.

3-phenyl-2-(2-trifluoromethylphenyl)-1,3-thiazolidin-4-one (**1a**). Yield: (82%); R_f = 0.463; m.p. 117-120 ^oC; IR: cm^{-1} 1683.9 (C=O); ^1H NMR ($CDCl_3$): 7.65-7.12 (9H, aromatics), 6.62 (1H, s, C2), 4.00 (1H, dd, C5, J = 1.4 Hz, and J = 15.8 Hz), 3.87 (1H, d, C5, J = 15.9 Hz); ^{13}C NMR: 171.18 (C4), 139.11, 137.24, 132.82, 129.14, 128.55, 127.34, 126.99, 126.98 (q, J = 30.8 Hz), 126.06 (q, J = 6.4 Hz), 124.92, 124.01 (q, J = 274.2 Hz), 60.15 (d, J = 1.5 Hz, C2), 33.02 (C5); MS: (m/z) 324 ($[M+H]^+$), $C_{16}H_{13}ONSF_3$ (324.07).

2-(2-chlorophenyl)-3-phenyl-1,3-thiazolidin-4-one (1c). Yield (75%); R_f = 0.580; m.p. 90-92 ^oC; IR: cm^{-1} 1684.2 (C=O), 1053.3 (S=O); ^1H NMR ($CDCl_3$): 7.34 – 7.11 (9 H, aromatics), 6.56 (1H, s, C2), 3.91 (1H, dd, C5, J = 1.2 Hz and J = 15.8 Hz), 3.78 (1H, d, C5, J = 15.7 Hz); ^{13}C NMR: 171.30 (C4), 137.56, 137.06, 132.43, 130.23, 129.72, 129.14, 127.49, 127.09, 126.69, 124.08, 61.63 (C2), 33.01 (C5); MS: (m/z) 290 ($[M+H]^+$), $C_{15}H_{13}ONSCl$ (290.04).

2-(2-fluorophenyl)-3-phenyl-1,3-thiazolidin-4-one (**1d**). Yield (83%); R_f = 0.326; m.p. 137-138 ^oC; IR: cm^{-1} 1667.9 (C=O), 1055.8 (S=O); ^1H NMR ($CDCl_3$): 7.35 – 6.99 (9 H, aromatics), 6.42 (1H, d, C2, J = 1.5 Hz), 4.03 (1H, dd, C5, J = 1.6 Hz and J = 17.4 Hz), 3.86 (1H, d, C5, J = 17.4 Hz); ^{13}C NMR: 171.00 (C4), 160.26 (d, J = 246.7), 137.41, 130.59 (d, J = 7.8 Hz), 129.27, 128.12 (d, J = 3.0 Hz), 127.19, 127.03, 125.17, 124.68 (d, J = 4.1 Hz), 116.08 (d, J = 20.1 Hz), 59.35 (d, C2, J = 3.1 Hz), 33.40 (C5); MS: (m/z) 274 ($[M+H]^+$), $C_{15}H_{13}ONSF$ (274.33).

2-(2-bromophenyl)-3-phenyl-1,3-thiazolidin-4-one (**1e**). Yield (81%); R_f = 0.461; m.p. 90-91 ^oC; IR: cm^{-1} 1683.9 (C=O), 1052.8 (S=O); ^1H NMR ($CDCl_3$): 7.55 – 7.11 (9 H, aromatics), 6.55 (1H, s, C2), 3.93 (1H, d, C5, J = 15.6 Hz), 3.80 (1H, d,

C5, J = 15.6 Hz); ^{13}C NMR: 171.49 (C4), 138.64 (br), 137.62, 133.53, 130.02, 129.22, 128.20, 126.95 (br), 126.71, 124.01, 122.50, 64.28 (C2), 32.98 (C5); MS: (m/z) 334 ($[M+H]^+$), $C_{15}H_{13}ONSBr$ (334.24).

2-(2-methylphenyl)-3-phenyl-1,3-thiazolidin-4-one (**1f**). Yield (60%); R_f = 0.531; m.p. 80-82 ^oC; IR: cm^{-1} 1682.5 (C=O), 1048.4 (S=O); ^{1}H NMR ($CDCl_3$): 7.34 – 7.11 (9 H, aromatics), 6.35 (1H, d, C2, J = 0.7 Hz), 3.94 (1H, dd, C5, J = 1.6 Hz and J = 16.0 Hz), 3.81 (1H, d, C5, J = 16.1 Hz); ^{13}C NMR: 171.42 (C4), 137.93, 137.40, 134.93, 131.19, 129.50, 129.11, 126.77, 126.68, 125.71, 124.40, 62.13 (C2), 33.13 (C5), 19.11 (CH_3); MS: (m/z) 286 ($[M+H]^+$), $C_{16}H_{16}ONS$ (270.37).

2-(2-methoxyphenyl)-3-phenyl-1,3-thiazolidin-4-one (**1g**). Yield (35%); R_f = 0.343; m.p. 82-84 ^oC; IR: cm^{-1} 1679.8 (C=O), 1027.7 (S=O); ^{1}H NMR ($CDCl_3$): 7.34 – 6.88 (9H, aromatics), 6.46 (1H, d, C2, J = 1.0 Hz), 3.95 (1H, dd, C5, J = 1.4 Hz and J = 15.8 Hz), 3.88 (3H, OCH_3), 3.78 (1H, d, C5, J = 15.5 Hz); ^{13}C NMR: 171.69 (C4), 156.50, 138.05, 129.81, 129.06, 128.02, 126.59, 124.49, 120.83, 111.06, 60.40 (C2), 55.69 (OCH_3), 33.43 (C5); MS: (m/z) 286 ($[M+H]^+$), $C_{16}H_{16}O_2NS$ (286.37).

2-(2-nitrophenyl)-3-phenyl-1,3-thiazolidin-4-one (**1h**). Yield (72%); R_f = 0.424; m.p. 137-138 ^oC; IR: cm^{-1} 1683.8 (C=O), 1062.4 (br, S=O); ^{1}H NMR ($CDCl_3$): 8.12 – 7.17 (9 H, aromatics), 6.81 (1H, d, C2, J = 1.0 Hz), 3.89 (1H, dd, J = 1.2 Hz and J = 16.2 Hz), 3.77 (1H, d, C5, J = 16.2 Hz); ^{13}C NMR: 171.91 (C4), 146.86, 137.66, 136.92, 134.65, 129.58, 129.52, 127.12, 126.83, 126.26, 124.11, 60.99 (C2), 32.70 (C5); MS: (m/z) 301 ($[M+H]^+$), $C_{15}H_{13}O_3N_2S$ (317.34).

4.2 General Procedure for the RT Synthesis of Thiazolidin-4-one Sulfoxides via Oxone®

Thiazolidin-4-one (1.01 mmol) was typically dissolved in methanol (8.0 mL), to which an aqueous solution of Oxone® (461 mg, 3.03 mmol calculated as $KHSO_5$, 152.2 g mol^{-1}, in 4.0 mL water) was added dropwise at room temperature with vigorous stirring. After the addition, the reaction mixture was stirred for 1 h. Complete conversion of the thiazolidin-4-one was established by thin layer chromatography. Water (40 mL) was then added to the mixture to dissolve precipitates, and the mixture was extracted with $CHCl_3$ (3 x 15 mL). The combined $CHCl_3$ layers were dried with Na_2SO_4, and the $CHCl_3$ was removed *in vacuo* followed by chromatography. All product sulfoxides with the exception of **5d** were isolated as a mixture of two diastereomeric isomers which were evident by ^{1}H NMR, and ratios of the two isomers were calculated by integration of the hydrogens on C2.

Sulfoxide-3-phenyl-2-(2-trifluoromethylphenyl)-1,3-thiazolidin-4-one (**2a**). Yield: (98%); R_f = 0.199; IR cm^{-1} 1696.0 (C=O), 1053.3 (S=O); ^{1}H NMR ($CDCl_3$), 7.81 – 7.05 (9 H, aromatics). Major isomer (75%), 6.22 (1H, s, C2), 4.01 (1H, d, C5, J = 17.3 Hz), 3.63 (1H, dd, C5, J = 0.4 Hz and J = 17.4 Hz). Minor isomer (25%), 5.23 (1H, s, C2), 4.08 (1H, d, C5, J = 16.9 Hz), 3.78 (1H, d, C5, J = 17.3 Hz); ^{13}C NMR: 168.66 (major C4), 168.40 (minor C4), 137.41, 136.62, 133.28, 131.96, 131.67, 130.24, 129.40, 129.14 (q, J = 26.3 Hz), 128.06 (q, J = 33.3 Hz), 127.77 (q, J = 5.4 Hz), 127.21, 126.88, 126.80, 126.45, 126.06 (q, J = 5.3 Hz), 124.16 (q, minor CF_3, J = 274.2 Hz), 123.86 (q, major CF_3, J = 275.5 Hz), 123.55 (q, J = 273.5 Hz), 123.42 (q, J = 3.3 Hz), 123.55, 85.85 (major C2), 75.41 (minor C2), 54.75 (minor C5), 52.19 (major C5); MS: (m/z) 340 ($[M+H]^+$), $C_{16}H_{13}O_2NSF_3$ (340.06).

Sulfoxide-2,3-diphenyl-1,3-thiazolidin-4-one (**2b**). Yield (96%); R_f = 0.159; m.p. 163-164 ^oC: IR: cm^{-1} 1681.8 (C=O), 1050.5 (S=O); ^{1}H NMR ($CDCl_3$): 7.50 – 7.21 (10 H, aromatics). Major isomer (98%), 5.97 (1H, s, C2), 3.90 (1H, d, C5, J = 17.0 Hz), 3.58 (1H, dd, C5, J = 1.2 Hz and J = 16.9 Hz). Minor isomer (2%), 6.07 (1H, s, C2), 3.98 (1H, d, C5, J = 16.6 Hz), 3.79 (1H, d, C5, J = 16.6 Hz); ^{13}C NMR: 168.41 (C4), 138.04, 130.73, 130.03, 129.92, 129.36, 127.01, 126.38, 123.50, 86.41 (C2), 52.28 (C5); MS: (m/z) 272 ($[M+H]^+$), $C_{15}H_{14}O_2NS$ (272.07).

Sulfoxide-2-(2-chlorophenyl)-3-phenyl-1,3-thiazolidin-4-one (2c). Yield (99%); R_f = 0.158; m.p. 60-62 ^oC; IR: cm^{-1} 1699.6 (C=O), 1044.5 (S=O); ^{1}H NMR ($CDCl_3$): 7.58 – 7.15 (9 H, aromatics). Major isomer (93%), 6.29 (1H, s, C2), 3.85 (1H, d, C5, J = 16.9 Hz), 3.64 (1H, dd, C5, J = 1.3 Hz and J = 17.1 Hz). Minor isomer (6%), 5.32 (1H, s, C2), 4.11 (1H, d, C5, J = 16.9 Hz), 3.86 (1H, d, C5, J = 17.0 Hz); ^{13}C NMR: 168.96 (C4), 137.87, 133.72, 131.42, 131.15, 131.04, 129.86, 129.53, 129.18, 128.32, 128.26, 127.22, 127.11, 126.96, 126.64, 124.41, 123.40, 84.32 (C2), 54.32 (C5 minor), 52.60 (C5 major); MS: (m/z) 306 ($[M+H]^+$), $C_{15}H_{13}O_2NSCl$ (306.04).

Sulfoxide-2-(2-fluorophenyl)-3-phenyl-1,3-thiazolidin-4-one (**2d**). Yield (99%); R_f = 0.098; m.p. 179-180 ^oC; IR: cm^{-1} 1682.9 (C=O), 1052.8 (S=O); ^{1}H NMR ($CDCl_3$): 7.48 – 6.20 (9 H, aromatics). Major isomer (89%), 6.15 (1H, s, C2), 3.91 (1H, d, C5, J = 17.0 Hz), 3.63 (1H, dd, C5, J = 0.5 Hz and J = 17.1 Hz). Minor isomer (11%), 5.29 (1H, s, C2), 4.06 (1H, d, C5, J = 16.7 Hz), 3.81 (1H, d, C5, J = 16.9 Hz); ^{13}C NMR: 168.54 (C4), 160.17 (d, J = 249.0 Hz), 137.70, 132.16 (d, J = 8.6 Hz), 130.50, 129.81, 129.52, 129.20, 127.34, 127.11, 126.89 (d, J = 1.5 Hz), 125.54 (d, J = 2.9), 124.59, 123.82, 115.72 (d, J = 19.8 Hz), 81.58 (C2), 52.91 (C5); MS: (m/z) 290 ($[M+H]^+$), $C_{15}H_{13}O_2NSF$ (290.07).

Sulfoxide-2-(2-bromophenyl)-3-phenyl-1,3-thiazolidin-4-one (**2e**). Yield (83%); R_f = 0.135; m.p. 154-155 ^oC; IR: cm^{-1} 1699.5 (C=O), 1044.1 (S=O); ^{1}H NMR ($CDCl_3$): 7.65 – 7.14 (9 H, aromatics). Major isomer (82%), 6.16 (1H, s, C2), 3.78 (1H, d, C5, J = 17.8 Hz), 3.54 (1H, dd, C5, J = 1.0 Hz and J = 17.2 Hz). Minor isomer (18%), 5.20 (1H, s, C2), 4.06 (1H, d,

C5, J = 16.8 Hz), 3.73 (1H, d, C5, J = 17.3 Hz); ^{13}C NMR: 169.14 (C4), 138.00, 134.48, 133.28, 131.68, 131.52, 129.91, 129.62, 129.29, 128.91, 127.80, 127.27, 127.04, 126.95, 124.46, 123.92, 123.37, 86.57 (C2 major), 78.70 (C2 minor), 54.43 (C5 minor), 52.43 (C5 major); MS: (m/z) 350 ($[M+H]^+$), $C_{15}H_{13}O_2NSBr$ (349.99).

Sulfoxide-2-(2-methylphenyl)-3-phenyl-1,3-thiazolidin-4-one (**2f**). Yield (99%); R_f = 0.154; m.p. 172-174 ^oC; IR: cm^{-1} 1694.2 (C=O), 1055.2 (S=O); ^{1}H NMR ($CDCl_3$): 7.44 – 7.22 (9 H, aromatics). Major isomer (94%), 6.07 (1H, s, C2), 3.90 (1H, d, C5, J = 16.9 Hz), 3.59 (1H, dd, C5, J = 1.1 Hz and J = 17.2 Hz), 2.60 (3H, s, CH_3). Minor isomer (6%), 5.29 (1H, s, C2), 4.03 (1H, d, C5, J = 16.1 Hz), 3.81 (1H, d, C5, J = 16.4 Hz), 2.49 (3 H, s, CH_3); ^{13}C NMR: 168.72 (C4 major), 167.27 (C4 minor), 138.18, 136.36, 131.98, 131.02, 130.04, 129.76, 129.70, 129.40, 129.09, 128.91, 128.44, 127.48, 127.01, 126.86, 126.49, 126.31, 124.77, 124.28, 123.36, 84.64 (C2), 53.47 (C5 minor), 52.45 (C5 major), 19.46 (CH_3); MS: (m/z) 286 ($[M+H]^+$), $C_{16}H_{16}O_2NS$ (286.36).

Sulfoxide-2-(2-methoxyphenyl)-3-phenyl-1,3-thiazolidin-4-one (**2g**). Yield (99%); R_f = 0.084; m.p. 184-185 ^oC; IR: cm^{-1} 1700.0 (C=O), 1059.0 (S=O); ^{1}H NMR ($CDCl_3$): 7.50 – 7.03 (9H, aromatics). Major isomer (85%), 6.23 (1H, s, C2), 4.03 (3H, s, OCH_3), 3.87 (1H, d, C5, J = 17.2 Hz), 3.60 (1H, d, C5, J = 17.0 Hz). Minor isomer (15%), 5.34 (1H, s, C2), 3.97 and 3.82 (4H, OCH_3 and C5) 3.54 (1H, d, C5, J = 18.6 Hz); ^{13}C NMR: 169.02 (C4), 156.84, 138.18, 131.53, 131.22, 129.61, 129.40, 129.12, 126.99, 126.15, 124.35, 123.29, 121.53, 120.96, 119.90, 118.79, 111.32, 110.83, 82.76 (C2), 55.95 (OCH_3), 53.83 (C5 minor), 53.05 (C5 major); MS: (m/z) 302 ($[M+H]^+$), $C_{16}H_{16}O_3NS$ (302.37).

Sulfoxide-2-(2-nitrophenyl)-3-phenyl-1,3-thiazolidin-4-one (**2h**). Yield (98%); R_f = 0.167; m.p. 78-79 ^oC; IR: cm^{-1} 1696.8 (C=O), 1055.8 (br, S=O); ^{1}H NMR ($CDCl_3$): 8.40 – 7.21 (9 H, aromatics). Major isomer (71%), 6.68 (1H, s, C2), 3.84 (1H, d, C5, J = 17.2 Hz), 3.68 (1H, d, J = 16.9 Hz). Minor isomer (29%), 5.32 (1H, s, C2), 4.13 (1H, d, C5, J = 16.5 Hz), 3.65 (1H, d, J = 16.6 Hz); ^{13}C NMR: 168.73 (C4 major), 166.74 (C4 minor), 148.83, 146.98, 137.64, 137.00, 135.57, 134.05, 131.38, 130.80, 130.38, 129.68, 129.49, 127.56, 127.28, 125.90, 124.80, 124.01, 123.88, 83.96 (C2 major), 75.26 (C2 minor), 53.45 (C5 minor), 52.65 (C5 major); MS: (m/z) 317 ($[M+H]^+$), $C_{15}H_{13}O_4N_2S$ (317.33).

Sulfoxide-2-(4-fluorophenyl)-3-phenyl-1,3-thiazolidin-4-one (**5a**). Yield (97%); R_f = 0.160; m.p. 192-194 ^oC; IR: cm^{-1} 1697.6 (C=O), 1048.3 (S=O); ^{1}H NMR ($CDCl_3$): 7.38 – 6.98 (9 H, aromatics). Major isomer (95%), 5.93 (1H, s, C2), 3.86 (1H, d, C5, J = 17.1 Hz), 3.56 (1H, dd, C5, J = 1.2 Hz and J = 17.2 Hz). Minor isomer (5%), 5.25 (1H, s, C2), 3.96 (1H, d, C5, J = 16.8 Hz), 3.76 (1H, d, C5, J = 16.9 Hz); ^{13}C NMR: 168.33 (C4 major), 167.66 (C4 minor), 163.72 (minor, d, J = 250.6 Hz), 163.49 (major, d, J = 250.6 Hz), 137.90, 136.75, 131.04 (d, J = 7.8 Hz), 129.55, 129.19, 128.43 (d, J = 7.7 Hz), 127.28, 127.14, 126.71 (d, J = 2.1), 124.97, 123.60, 117.24 (d, J = 22.2 Hz), 116.22 (d, J = 22.3 Hz), 85.84 (C2), 53.82 (C5 minor), 52.91 (C5 major); MS: (m/z) 290 ($[M+H]^+$), $C_{15}H_{13}O_2NSF$ (290.07).

Sulfoxide-2-(4-bromophenyl)-3-phenyl-1,3-thiazolidin-4-one (**5b**). Yield (98%); R_f = 0.183; m.p. 67-68 ^oC; IR: cm^{-1} 1698.4 (C=O), 1050.2 (S=O); ^{1}H NMR ($CDCl_3$): 7.58 – 7.21 (9 H, aromatics). Major isomer (98%), 6.07 (1H, s, C2), 3.94 (1H, d, C5, J = 17.4 Hz), 3.64 (1H, dd, C5, J = 0.9 Hz and J = 17.0 Hz). Minor isomer (2%), 5.29 (1H, s, C2), 4.07 (1H, d, C5, J = 16.9 Hz), 3.79 (1H, d, C5, J = 16.6 Hz); ^{13}C NMR: Major isomer, 168.23 (C4), 137.57, 132.76, 129.70, 129.19, 127.98, 126.87, 123.85, 123.27, 85.29 (C2), 52.01 (C5). Minor isomer, 167.95 (C4), 136.51, 131.71, 130.55, 128.81, 127.64, 126.69, 124.78, 124.07, 85.29 (C2), 53.87 (C5); MS: (m/z) 350 ($[M+H]^+$), $C_{15}H_{13}O_2NSBr$ (349.99).

Sulfoxide-2-(4-methoxyphenyl)-3-phenyl-1,3-thiazolidin-4-one (**5c**). Yield (99%); R_f = 0.103; m.p. 156-157 ^oC; IR: cm^{-1} 1705.2 (C=O), 1051.9 (S=O); ^{1}H NMR ($CDCl_3$): 7.42 – 6.82 (9H, aromatics). Major isomer (86%), 5.94 (1H, s, C2), 3.90 (1H, d, C5, J = 17.4 Hz), 3.78 (3H, s, OCH_3), 3.54 (1H, dd, C5, J = 1.2 Hz and J = 17.0 Hz). Minor isomer (14%), 5.26 (1H, s, C2), 3.96 (1H, d, C5, J = 17.0 Hz), 3.78 and 3.71 (4H, OCH_3 and C5); ^{13}C NMR: Major isomer, 168.34 (C4), 160.71, 138.04, 129.28, 127.73, 126.90, 123.43, 122.23, 115.25, 85.95 (C2), 55.45 (OCH_3), 52.17 (C5). Minor isomer, 167.71 (C4), 136.95, 130.30, 128.91, 126.76, 124.89, 120.00, 114.28, 85.95 (C2), 55.20 (OCH_3), 53.65 (C5); MS: (m/z) 302 ($[M+H]^+$), $C_{16}H_{16}O_3NS$ (302.37).

Sulfoxide-2-(2-nitrophenyl)-3-phenyl-1,3-thiazolidin-4-one (**5d**). Yield (77%); R_f = 0.075; m.p. d 213 ^oC; IR: cm^{-1} 1701.3 (C=O), 1051.8 (S=O); ^{1}H NMR ($CDCl_3$): 8.35 – 7.27 (9 H, aromatics). 6.04 (1H, s, C2), 3.99 (1H, d, C5, J = 17.2 Hz), 3.69 (1H, dd, J = 0.8 Hz and 17.4 Hz); ^{13}C NMR: 168.15 (C4), 148.98, 138.14, 137.58, 129.86, 127.76, 127.67, 125.32, 123.74, 86.12 (C2), 52.62 (C5); MS: (m/z) 317 ($[M+H]^+$), $C_{15}H_{13}O_4N_2S$ (317.33).

4.3 General Procedure for the Synthesis of Thiazolidin-4-One Sulfones via $KMnO_4$

Thiazolidin-4-one (0.553 mmol) was dissolved in glacial acetic acid (2.4 mL), to which an aqueous solution of $KMnO_4$ (175 mg, 1.11 mmol, in 3.0 mL water) was added dropwise at room temperature with vigorous stirring, and stirred an additional 5 m. Solid sodium bisulfite ($NaHSO_3/Na_2S_2O_5$) was then added until the solution remained colorless; 3.0 mL of water was then added to the mixture and stirred for 10 m. Most crude products were isolated as powders by filtration and water rinses; products were purified by recrystallization in CH_3OH. Products **3a**, **3c**, and **3e** were not isolated as powders, but rather by

extraction of the reaction mixture with toluene (3 x 10 mL). The combined toluene layers were dried with Na_2SO_4, and toluene was removed *in vacuo* followed by chromatography.

Sulfone-3-phenyl-2-(2-trifluoromethylphenyl)-1,3-thiazolidin-4-one (**3a**). Yield: (73%); oil; R_f = 0.314; IR cm^{-1} 1705.2 (C=O), 1128.2, 1120.4 (S=O); ^{1}H NMR ($CDCl_3$), 7.76 – 7.20 (9 H, aromatics), 6.52 (1H, s, C2), 4.15 (1H, d, C5, J = 16.8 Hz), 4.09 (1H, d, C5, J = 16.8 Hz); ^{13}C NMR: 162.45 (C4), 135.66, 132.86, 130.72, 129.91 (q, J = 31.1 Hz), 129.58, 128.45, 128.19, 127.85, 127.21 (br q, J = 6.0 Hz), 125.25, 123.67 (q, J = 274.3 Hz), 80.01 (C2), 50.97 (C5); MS: (m/z) 356 ($[M+H]^+$), $C_{16}H_{13}O_3NSF_3$ (356.06).

Sulfone-2,3-diphenyl-1,3-thiazolidin-4-one (**3b**). Yield (76%); R_f = 0.366; m.p. 178-180 ^{o}C: IR: cm^{-1} 1693.1 (C=O), 1141.6, 1125.2 (S=O); ^{1}H NMR ($CDCl_3$): 7.47 – 7.18 (10 H, aromatics), 5.99 (1H, s, C2), 3.88 (1H, d, C5, J = 16.9 Hz), 3.56 (1H, dd, C5, J = 1.2 Hz and J = 17.1 Hz); ^{13}C NMR: 162.58 (C4), 136.25, 130.87, 129.62, 129.58, 129.01, 128.05, 125.13, 83.92 (C2), 50.70 (C5); MS: (m/z) 288 ($[M+H]^+$), $C_{15}H_{14}O_3NS$ (288.07).

Sulfone-2-(2-chlorophenyl)-3-phenyl-1,3-thiazolidin-4-one (3c). Yield (69%); oil; R_f = 0.328; IR: cm^{-1} 1717.6 (C=O), 1140.6, 1097.0 (S=O); ^{1}H NMR ($CDCl_3$): 7.53 – 7.26 (9 H, aromatics), 6.65 (1H, s, C2), 4.10 (1H, d, C5, J = 16.9 Hz), 4.05 (1H, d, C5, J = 16.6 Hz); ^{13}C NMR: 162.50 (C4), 136.12, 135.29 (br), 131.80, 130.93 (br), 129.64, 128.05, 127.85, 127.65, 127.54 (br), 124.74, 80.48 (C2), 50.78 (C5); MS: (m/z) 322 ($[M+H]^+$), $C_{15}H_{13}O_3NSCl$ (322.03).

Sulfone-2-(2-fluorophenyl)-3-phenyl-1,3-thiazolidin-4-one (**3d**). Yield (76%); m.p. 159-160 ^{o}C; IR: cm^{-1} 1686.5 (C=O), 1136.0, 1127.2 (S=O); ^{1}H NMR ($CDCl_3$): 7.53 – 7.22 (9 H, aromatics), 6.27 (1H, s, C2), 4.17 (1H, d, C5, J = 16.9 Hz), 4.10 (1H, d, C5, J = 17.0 Hz); ^{13}C NMR: 162.40 (C4), 161.49 (d, J = 250.9), 135.99, 132.87 (d, J = 7.8 Hz), 129.75, 128.98, 128.38, 125.34, 125.24 (d, J = 3.1 Hz), 117.70 (d, J = 11.7), 116.85 (d, J = 20.8 Hz), 79.78 (C2), 51.26 (C5); MS: (m/z) 306 ($[M+H]^+$), $C_{15}H_{13}O_3NSF$ (306.06).

Sulfone-2-(2-bromophenyl)-3-phenyl-1,3-thiazolidin-4-one (**3e**). Yield (91%); oil; R_f = 0..270; IR: cm^{-1} 1718.3 (C=O), 1141.5, 1097.8 (S=O); ^{1}H NMR ($CDCl_3$): 7.70 – 7.16 (9 H, aromatics), 6.68 (1H, s, C2), 4.09 (1H, d, C5, J = 16.9 Hz), 4.04 (1H, d, C5, J = 16.9 Hz); ^{13}C NMR: 162.44 (C4), 136.09, 134.15, 131.98, 129.60, 129.15, 129.01, 128.40, 127.97, 127.82, 124.68, 83.79 (C2), 50.87 (C5); MS: (m/z) 366 ($[M+H]^+$), $C_{15}H_{13}O_3NSBr$ (365.98).

Sulfone-2-(2-methylphenyl)-3-phenyl-1,3-thiazolidin-4-one (**3f**). Yield (70%); m.p. 143-144 ^{o}C; IR: cm^{-1} 1698.5 (C=O), 1129.0, 1100.5 (S=O); ^{1}H NMR ($CDCl_3$): 7.39 – 7.25 (9H, aromatics), 6.27 (1H, s, C2), 4.08 (1H, d, C5, J = 16.3 Hz), 4.00 (1H, d, C5, J = 16.8 Hz), 2.50 (3H, s, CH_3); ^{13}C NMR: 162.73 (C4), 138.21, 136.61, 131.98, 130.50, 129.60, 127.96, 127.14, 125.64, 124.71, 81.20 (C2), 50.56 (C5), 20.00 (CH_3); MS: (m/z) 302 ($[M+H]^+$), $C_{16}H_{16}O_3NS$ (302.32).

Sulfone-2-(2-methoxyphenyl)-3-phenyl-1,3-thiazolidin-4-one (**3g**). Yield (80%); m.p. 130-131 ^{o}C; IR: cm^{-1} 1699.6 (C=O), 1141.9, 1127.7 (S=O); ^{1}H NMR ($CDCl_3$): 7.46 – 7.00 (9H, aromatics), 6.32 (1H, vbr s, C2,), 4.05 (1H, d, C5, J = 16.5 Hz), 3.96 (1H, d, C5, J = 17.0 Hz), 3.93 (3H, s, OCH_3); ^{13}C NMR: 162.94 (C4), 158.28, 136.59, 132.16, 129.56, 128.00, 125.13 (br), 121.32, 118.62, 111.85, 80.48 (vbr, C2), 56.04 (OCH_3), 51.19 (br, C5); MS: (m/z) 318 ($[M+H]^+$), $C_{16}H_{16}O_4NS$ (318.36).

Sulfone-2-(2-nitrophenyl)-3-phenyl-1,3-thiazolidin-4-one (**3h**). Yield (63%); m.p. 177-179 ^{o}C; IR: cm^{-1} 1709.0 (C=O), 1158.8, 1120.2 (S=O); ^{1}H NMR ($CDCl_3$): 8.38 – 7.27 (9H, aromatics), 7.19 (1H, s, C2), 4.03 (1H, d, C5, J = 16.4 Hz), 3.94 (1H, d, C5, J = 17.1 Hz); ^{13}C NMR: 162.64 (C4), 148.34, 136.48, 135.09, 131.69, 129.91, 128.35, 127.27, 127.22, 127.12, 124.62, 80.98 (C2), 50.69 (C5); MS: (m/z) 333 ($[M+H]^+$), $C_{15}H_{13}O_5N_2S$ (333.32).

Sulfone-2-(4-fluorophenyl)-3-phenyl-1,3-thiazolidin-4-one (**6a**). Yield (81%); m.p. 186-187 ^{o}C; IR: cm^{-1} 1723.8 (C=O), 1189.3, 1095.9 (S=O); ^{1}H NMR ($CDCl_3$): 7.35 – 7.07 (9 H, aromatics), 5.96 (1H, s, C2), 4.02 (2H, s); ^{13}C NMR: 163.93 (d, J = 303.1), 162.93 (C4), 135.93, 130.37 (d, J = 8.9 Hz), 129.68, 128.22, 125.28, 124.41 (d, J = 3.1 Hz), 116.92 (d, J = 22.0 Hz), 83.04 (C2), 50.88 (C5); MS: (m/z) 306 ($[M+H]^+$), $C_{15}H_{13}O_3NSF$ (306.06).

Sulfone-2-(4-bromophenyl)-3-phenyl-1,3-thiazolidin-4-one (**6b**). Yield (78%); m.p. 177-178 ^{o}C; IR: cm^{-1} 1680.6 (C=O), 1127.4, 1104.0 (S=O); ^{1}H NMR ($CDCl_3$): 7.61 – 7.27 (9 H, aromatics), 6.02 (1H, s, C2), 4.08 (2H, s); ^{13}C NMR: 162.39 (C4), 135.84, 132.82, 129.81, 129.65, 128.18, 127.66, 125.38, 125.15, 83.07 (C2), 50.84 (C5); MS: (m/z) 366 ($[M+H]^+$), $C_{15}H_{13}O_3NSBr$ (365.98).

Sulfone-2-(4-methoxyphenyl)-3-phenyl-1,3-thiazolidin-4-one (**6c**). Yield (88%); m.p. 124-127 ^{o}C; IR: cm^{-1} 1708.2 (C=O), 1121.0, 1100.4 (S=O); ^{1}H NMR ($CDCl_3$): 7.35 – 6.92 (9H, aromatics), 5.98 (1H, s, C2,), 4.07 (1H, d, C5, J = 16.2 Hz), 4.02 (1H, d, C5, J = 16.8 Hz), 3.80 (3H, s, OCH_3); ^{13}C NMR: 162.61 (C4), 161.42, 136.11, 129.68, 129.46, 127.92, 125.28, 120.12, 114.96, 83.34 (C2), 55.48 (OCH_3), 50.70 (C5); MS: (m/z) 318 ($[M+H]^+$), $C_{16}H_{16}O_4NS$ (318.36).

Sulfone-2-(4-nitrophenyl)-3-phenyl-1,3-thiazolidin-4-one (**6d**). Yield (82%); m.p. 204-206 ^{o}C; IR: cm^{-1} 1698.8 (C=O), 1130.7, 1113.9 (S=O); ^{1}H NMR ($CDCl_3$): 8.32 – 7.28 (9H, aromatics), 6.17 (1H, s, C2), 4.17 (1H, d, C5, J = 16.9 Hz), 4.11

(1H, d, C5, J = 16.9 Hz); ^{13}C NMR: 162.06 (C4), 149.40, 135.53, 135.39, 129.89, 129.52, 128.50, 125.09, 124.68, 82.69 (C2), 51.18 (C5); MS: (m/z) 333 ($[M+H]^+$), $C_{15}H_{13}O_5N_2S$ (333.32).

*4.4 High Temperature Oxidation of Thiazolidin-4-Ones **1a-h** Using Oxone®*

Thiazolidin-4-one (**1a-h)** (0.103 mmol) was dissolved in refluxing MeOH (16 mL), to which a solution of Oxone® (1.251 g, 0.824 mmol, in 8 mL H_2O) was added dropwise with vigorous stirring. Then the reaction mixture was heated for 8 h. Upon cooling, 40 mL of H_2O was added and the solution was then extracted with CH_2Cl_2 (3 x 25 mL). The combined CH_2Cl_2 layers were dried with Na_2SO_4, and the CH_2Cl_2 was removed *in vacuo*. The resulting crude product mixture of sulfoxide and sulfone was purified using preparative chromatography plates (silica gel GF, 250 micron) purchased from Analtech (Rabel & Sherma, 2017). The product mixture was dissolved sparingly in CH_2Cl_2 and deposited on the preparative chromatography plates using a streaking apparatus purchased from the Aldrich Chemical Company. No more than 150 mg of product mixture was deposited on a plate. The plates were developed using 3:1 cyclohexane:ethyl acetate, after which the plates were air-dried. The location of the products' bands on the plate were identified by R_f values and fluorescent indicators present in the silica gel. The sulfoxide and sulfone bands were separated by scraping the bands of silica from the plate. The products were then isolated by extracting the collected silica with boiling ethyl acetate followed by filtration and removal of the ethyl acetate *in vacuo*. The molar ratios of either sulfoxide **2** to sulfone **3** or sulfoxide **5** to sulfone **6** were determined by the isolated yields of the two respective compounds based on the thiazolidin-4-one **1** as the limiting reagent.

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