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Selective Synthesis of Substituted 3-Aryl-2-phenyl-1,3-thiazolidin-4-one Sulfoxides and Sulfones by *S*-Oxidation with Oxone

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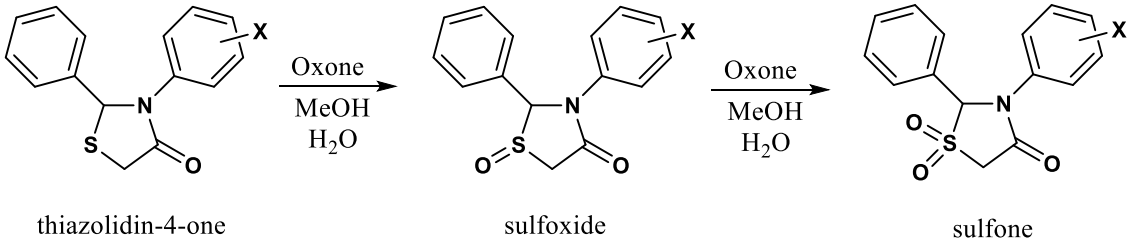
Abstract

S-oxidation of 3-aryl-2-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. Alternatively, the sulfone was prepared selectively in most of the compounds evaluated at high temperature by increasing the equivalents of Oxone® used; the extent of this selectivity was affected by the substituent and its position on the N3 aromatic ring. The ratio of the sulfoxide and sulfone products was quantified by isolating the products by liquid chromatography.



thiazolidin-4-one sulfoxide sulfone

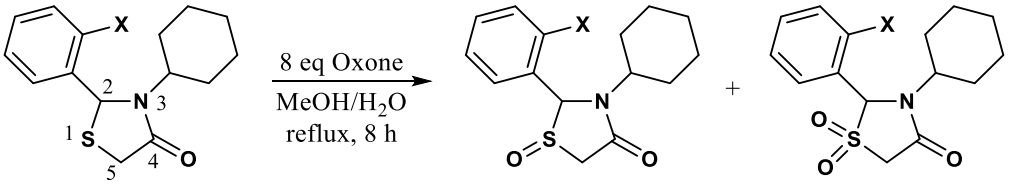
Keywords: thiazolidin-4-ones, oxone, sulfoxide, sulfone

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

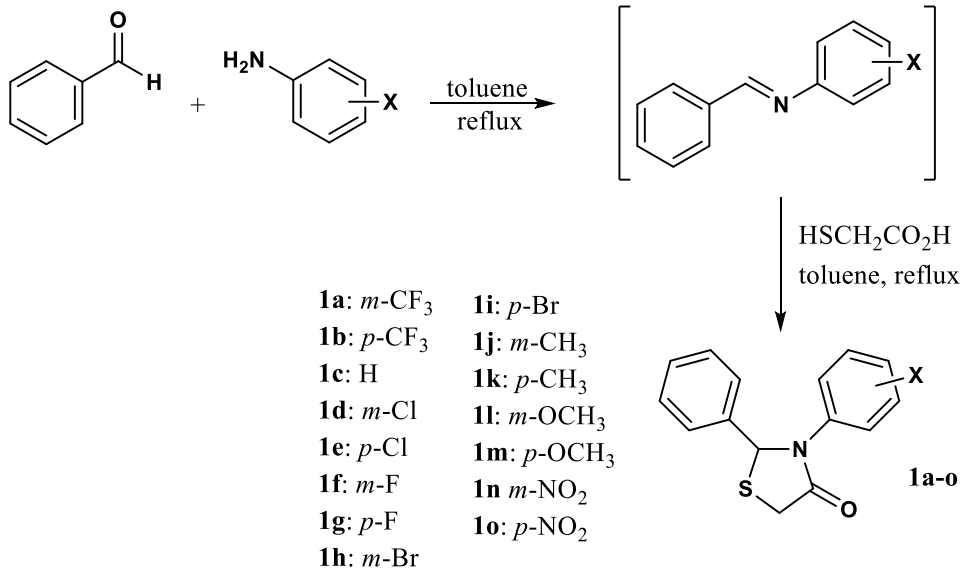
Scheme 1. Oxidation of thiazolidin-4-ones using high temperature Oxone®-based reaction conditions

In this study, we report the high temperature oxidation of a series of *meta- and para*-substituted 3-aryl-2-phenyl-1,3-thiazolidin-4-ones with Oxone® to determine if 1) substituents on the N3 aromatic ring affect oxidative selectivity and 2) compare the substituent effects on the N3 aromatic ring to those previously reported on the C2 aromatic ring. 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 Meta- and Para-Substituted Thiazolidin-4-Ones

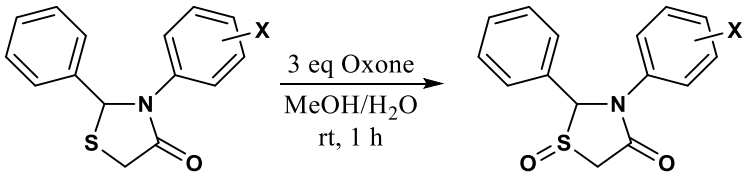
The *meta- and para*-substituted 3-aryl-2-phenyl-1,3-thiazolidin-4-ones **1c-o** used in this evaluation had been previously prepared by sequential condensation reactions.(Tierney et al., 2005) The *meta*- and *para*-CF_3-substituted compounds, **1a** and **1b,** were likewise prepared by condensation of benzaldehyde with the respective substituted 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 *meta*- and *para*-substituted 3-aryl-2-phenyl-1,3-thiazolidin-4-ones **1a-o**

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

Exclusive formation of sulfoxide compounds **2a-2o** was realized by performing the oxidation at room temperature with a 3 equivalents of Oxone®. (Scheme 3) The reaction time for sulfoxide formation was optimized at 1h to insure complete conversion of the thiazolidin-4-ones which was followed by thin layer chromatography (TLC). Results are summarized in Table 1. Oxidation of **1e** at extended reaction times showed no sulfone formation by ^{1}H NMR at periods as long as 25 h. 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).

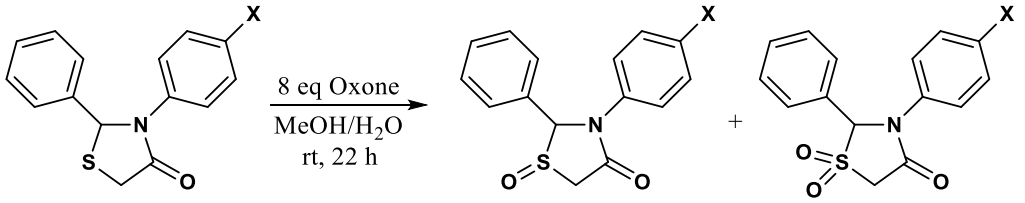


Scheme 3. Selective low temperature Oxone® oxidation of thiazolidin-4-ones to sulfoxides

Table 1. *Meta*- and *para*-substituted 3-aryl-2-phenyl-1,3-thiazolidin-4-one sulfoxides **2a-2o** synthesized according to Scheme 4

Product	% Yield	Melting Point (^{o}C)	R_f (3:1 cyclohexane:EtOAc)
2a, X = *m*-CF_3	98	64-65	0.066
2b, X = *p*-CF_3	94	182-183	0.138
2c, X = H	96	178-180	0.159
2d, X = *m*-Cl	74	166-168	0.160
2e, X = *p*-Cl	98	164-165	0.094
2f, X = *m*-F	99	149-152	0.137
2g, X = *p*-F	99	188-190	0.230
2h, X = *m*-Br	75	167-169	0.112
2i, X = *p*-Br	99	190-191	0.134
2j, X = *m*-CH_3	97	161-162	0.143
2k, X = *p*-CH_3	97	179-180	0.157
2l, X = *m*-OCH_3	99	d 219	0.56
2m, X = *p*-OCH_3	99	188-189	0.101
2n, X = *m*-NO_2	99	205-207	0.089
2o, X = *p*-NO_2	44	d 215	0.075

Room temperature oxidations with 8 equivalents of Oxone® were performed with compounds **1c** and **1e**.(Scheme 4) Although increasing both equivalents of Oxone® and reaction time did result in the formation of sulfones, yields were low and sulfoxide products were still significantly favored.



1c, X = H
1e, X = Cl

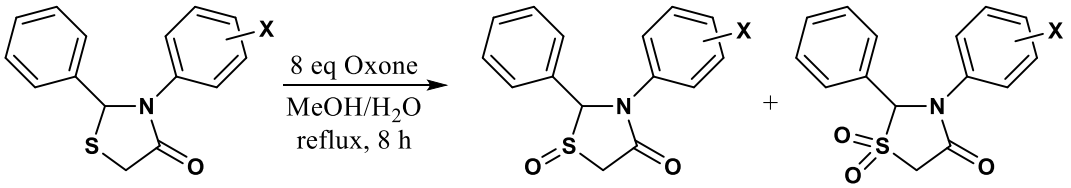
2c (80 %)
2e (67 %)

3c (9 %)
3e (8 %)

Scheme 4. Low temperature Oxone® oxidation using 8 equivalents of Oxone®

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

Compounds **1a-o** 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 determine if selective formation of sulfones could be realized according to the substituted N3 aromatic ring (Scheme 5). Results are presented in Table 2.



1a-o **2a-o** **3a-o**

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

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

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

Thiazolidin-4-one (**1**)	Sulfoxide:Sulfone (**2**:**3**)	Total Yield
1a, X = *m*-CF_3	1.0:2.9	43 %
1b, X = *p*-CF_3	1.0:2.0	40 %
1c, X = H	1.0:3.2	66 %
1d, X = *m*-Cl	1.0:2.0	67 %
1e, X = *p*-Cl	1.0:1.7	58 %
1f, X = *m*-F	1.0:1.6	71 %
1g, X = *p*-F	1.0:1.5	94 %
1h, X = *m*-Br	1.0:2.6	56 %
1i, X = *p*-Br	1.0:1.9	54 %
1j, X = *m*-CH_3	1.1:1.0	65 %
1k, X = *p*-CH_3	1.0:1.5	55 %
1l, X = *m*-OCH_3	sulfoxide only	14 %
1m, X = *p*-OCH_3	1.0:12.3	78 %
1n, X = *m*-NO_2	1.0:7.4	61 %
1o, X = *p*-NO_2	1.0:6.0	48 %

Results in Table 2 show that sulfone formation varied according to both the substituent and its position on the N3 aromatic ring. However, few clear substitution/reactivity correlations can be ascertained. The selectivity of sulfone versus sulfoxide formation was favored 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. Oxidation yields showed no correlation with substituent location: in two sets (X = F and OCH_3) the *para*-substituted compounds demonstrated higher yields, and in the remaining five sets the *meta*-substituted compounds demonstrated higher yields.

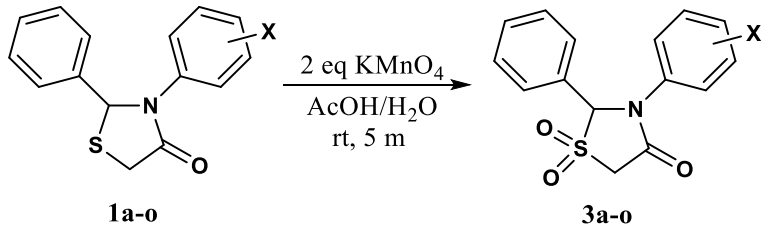
The effect of the substituents' electronic properties on yield somewhat mirrored previously reported oxidations of the 2-aryl-3-cyclohexyl-1,3-thiazolidin-4-ones with Oxone®, which also showed the highest sulfone selectivity for OCH_3

and NO_2 substituents (Cannon et al., 2015). The highest sulfone selectivity was observed for *p*-OCH_3 substituted compound **1m** (>12:1 sulfone:sulfoxide). High sulfone selectivity was also realized for both *meta*- and *para*-NO_2 substituted compounds **1n** and **1o,** respectively, and reasonable selectivity was seen for X = H (**1c**). However, there are significant differences between the 3-aryl-2-phenyl-1,3-thiazolidin-4-ones and
2-aryl-3-cyclohexyl-1,3-thiazolidin-4-ones as well. Higher sulfone selectivity was observed for all the halide- and CF_3-substituted 3-aryl-thiazolidin-4-ones versus the 3-cyclohexyl-thiazolidin-4-ones, while sulfone selectivity dropped dramatically for the CH_3-substituted 3-aryl-thiazolidin-4-ones. Thus, although the strongly electron donating *p*-OCH_3 and the strongly electron withdrawing NO_2 substituents still showed the best sulfone selectivity, all other substituents on the N3 aromatic ring demonstrated less variation amongst each other than was seen in the previous study with substituents on the C2 aromatic ring. This decreased variation is probably rooted in the more remote location of the N3 aromatic ring from the sulfur, which is expected to reduce the corresponding electronic effect of substituents on the N3 aromatic ring.

Overall, the total oxidation yields are lower for the 3-aryl-2-phenyl-1,3-thiazolidin-4-ones (average yield = 58 %) versus 2-aryl-3-cyclohexyl-1,3-thiazolidin-4-ones (average yield = 89 %) despite reactant conversions of 100% for all compounds evaluated. To determine if sulfones were stable under reaction conditions, isolated sulfone **3b** (*p*-CF_3) was subjected to 8 Oxone® equivalents in refluxing aqueous methanol for 8 h. No significant decomposition was detected by TLC, and **3b** was recovered quantitatively. Therefore, product decomposition cannot account for the observed lower yields.

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

Since exclusive formation of 3-aryl-2-phenyl-1,3-thiazolidin-4-one sulfones was not reliably realized using Oxone®, an alternative syntheses of the sulfones using aqueous $KMnO_4$ was evaluated.(Surrey, 1948) This method was applied to compounds **1a**-**1o** to produce the corresponding sulfones (Scheme 6); results are summarized in Table 3. Although no measures were taken to optimize this reaction, the oxidation yields are overall significantly higher for the 3-aryl-2-phenyl-1,3-thiazolidin-4-ones (average yield=76%) versus 2-aryl-3-cyclohexyl-1,3-thiazolidin-4-ones (average yield =56%) previously synthesized by this method (Cannon et al., 2015).



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

Table 3. *Meta*- and *para*-substituted 3-aryl-2-phenyl-1,3-thiazolidin-4-one sulfones **3a**-**3o** synthesized according to Scheme 6

Product	% Yield	Melting Point (°C)
3a, X = *m*-CF_3	78	106-110
3b, X = *p*-CF_3	81	186-187
3c, X = H	76	178-180
3d, X = *m*-Cl	82	183-184
3e, X = *p*-Cl	76	176-178
3f, X = *m*-F	77	171-172
3g, X = *p*-F	56	141-142
2h, X = *m*-Br	77	190-191
2i, X = *p*-Br	76	201-204
2j, X = *m*-CH_3	65	173-175
2k, X = *p*-CH_3	78	104-105
2l, X = *m*-OCH_3	83	214-217
2m, X = *p*-OCH_3	95	104-105
2n, X = *m*-NO_2	80	199-200
2o, X = *p*-NO_2	56	204-206

3. Conclusion

S-oxidation of 3-aryl-2-phenyl-1,3-thiazolidin-4-ones with Oxone® was dependent on the reaction temperature, equivalents of Oxone® used, the substituent, and its location on the N3 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. By increasing the amount of Oxone® to 8 equivalents, room temperature oxidation of two thiazolidin-4-ones (**1c** and **1e**) resulted in the formation of sulfone in yields <10 %; sulfoxide formation was still preferred. At high temperature 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 3-cyclohexyl-2-phenyl-1,3-thiazolidin-4-ones, exclusive formation of sulfone versus sulfoxide was never realized by Oxone® oxidation. Exclusive sulfone formation was best achieved using 2 equivalents of $KMnO_4$.

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 3-Aryl-Substituted -2-Phenyl-Thiazolidin-4-Ones

All thiazolidine-4-ones used in this study except the CF_3-substituted compounds had been previously synthesized and characterized. Thiazolidine-4-ones were prepared using the procedure previously described. (Tierney et al., 2005) Isolated yields of the CF_3-substituted thiazolidine-4-ones are based on the corresponding aniline as the limiting reactant. No attempt was made to maximize the product yields. The *p*-CF_3 compound **1b** was purified by recrystallization using methanol. The *m*-CF_3 compound **1a**, a colorless oil, was purified chromatography on pre-coated plates of silica gel GF 250 μm using 3:1 cyclohexane/EtOAc.

2-phenyl-2-(3-trifluoromethylphenyl)-1,3-thiazolidin-4-one (**1a**). Yield: (98%); R_f = 0.607; IR: cm^{-1} 1687.6 (C=O); ^1H NMR ($CDCl_3$): 7.42-7.14 (9H, aromatics), 6.04 (1H, s, C2), 3.89 (1H, dd, C5, J = 1.3 Hz, and J = 15.8 Hz), 3.77 (1H, d, C5, J = 15.8 Hz); ^{13}C NMR: 171.29 (C4), 138.62, 138.21, 131.51 (q, J = 32.8 Hz), 129.73, 129.34, 129.20, 128.78, 127.04, 123.90 (q, J = 272.8.0 Hz), 123.68 (q, J = 3.4 Hz), 122.22 (q, J = 4.0 Hz), 65.42 (C2), 33.52 (C5); MS: (m/z) 324 ($[M+H]^+$), $C_{16}H_{13}ONSF_3$ (324.07).

2-phenyl-2-(4-trifluoromethylphenyl)-1,3-thiazolidin-4-one (**1b**). Yield: (94%); R_f = 0.586; m.p. 107-108 ^oC; IR: cm^{-1} 1681.4 (C=O); ^1H NMR ($CDCl_3$): 7.46-7.17 (9H, aromatics), 6.17 (1H, s, C2), 3.99 (1H, dd, C5, J = 1.4 Hz, and J = 16.1 Hz), 3.86 (1H, d, C5, J = 16.4 Hz); ^{13}C NMR: 171.38 (C4), 140.87, 139.04, 129.30, 128.56 (q, J = 32.8 Hz), 126.76, 126.45 (q, J = 4.1 Hz), 124.95, 123.86 (q, J = 272.4 Hz), 65.19 (C2), 33.56 (C5); MS: (m/z) 324 ($[M+H]^+$), $C_{16}H_{13}ONSF_3$ (324.07).

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. 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. Except for compounds **2k** (*p*-Me) and **2o** (*p*-NO_2), two sets of diastereomeric isomers were evident by ^1H NMR and ratios were calculated by integration of the hydrogens on C2.

Sulfoxide-2-phenyl-2-(3-trifluoromethylphenyl)-1,3-thiazolidin-4-one (**2a**). Yield: (98%); R_f = 0.066; m.p. 64-65 ^oC; IR cm^{-1} 1703.9 (C=O), 1061.0 (S=O); ^1H NMR ($CDCl_3$), 7.58 – 7.32 (9 H, aromatics). Major isomer (95%), 6.03 (1H, s, C2), 3.87 (1H, d, C5, J = 17.0 Hz), 3.56 (1H, dd, C5, J = 1.3 Hz and J = 17.1 Hz). Minor isomer (5%), 6.10 (1H, s, C2), 3.98 (1H, d, C5, J = 17.0 Hz), 3.77 (1H, d, C5, J = 16.4 Hz); ^{13}C NMR: 168.66 (C4), 138.69, 137.57, 131.70 (q, J = 32.7 Hz), 130.30, 130.10, 129.96, 127.95, 126.23, 126.00, 124.93, 123.55 (q, J = 273.5 Hz), 123.42 (q, J = 3.3 Hz), 122.20,

119.98 (q, J = 3.6 Hz), 85.85 (C2), 52.19 (C5); MS: (m/z) 340 ($[M+H]^+$), $C_{16}H_{13}O_2NSF_3$ (340.06).

Sulfoxide-2-phenyl-2-(4-trifluoromethylphenyl)-1,3-thiazolidin-4-one (**2b**). Yield: (94%); R_f = 0.138; m.p. 182-183 ^oC; IR cm^{-1} 1693.6 (C=O), 1078.1 (S=O); ^1H NMR ($CDCl_3$), 7.58 – 7.32 (9 H, aromatics). Major isomer (93%), 6.06 (1H, s, C2), 3.88 (1H, d, C5, J = 17.2 Hz), 3.59 (1H, dd, C5, J = 1.4 Hz and J = 17.2 Hz). Minor isomer (7%), 6.11 (1H, s, C2), 4.00 (1H, d, C5, J = 17.1 Hz), 3.81 (1H, d, C5, J = 16.6 Hz); ^{13}C NMR: 168.69 (C4), 141.30, 130.39, 130.21, 130.13, 128.43 (q, J = 33.5 Hz), 126.74, 126.54 (q, J = 4.3 Hz), 125.05 (d, 18.6 Hz), 124.60, 123.79 (q, J = 271.5 Hz), 122.60, 122.44, 85.80 (C2), 52.33 (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 (**2c**). Yield (96%); R_f = 0.159; m.p. 163-164 ^oC: IR: cm^{-1} 1681.8 (C=O), 1050.5 (S=O); ^1H 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-3-(3-chlorophenyl)-2-phenyl-1,3-thiazolidin-4-one (2d). Yield (74%); R_f = 0.160; m.p. 166-168 ^oC; IR: cm^{-1} 1685.4 (C=O), 1053.3 (S=O); ^1H NMR ($CDCl_3$): 7.48 – 7.09 (9 H, aromatics). Major isomer (94%), 5.92 (1H, s, C2), 3.80 (1H, d, C5, J = 17.2 Hz), 3.49 (1H, dd, C5, J = 1.3 Hz and J = 17.2 Hz). Minor isomer (6%), 6.00 (1H, s, C2), 3.92 (1H, d, C5, J = 16.5 Hz), 3.70 (1H, d, C5, J = 16.5 Hz); ^{13}C NMR: 168.49 (C4), 167.78 (C4), 139.21, 138.09, 134.90, 134.47, 130.30, 130.20, 130.05, 129.89, 129.02, 128.93, 126.99, 126.25, 124.99, 123.36, 122.75, 121.03, 85.97 (C2), 52.21 (C5); MS: (m/z) 306 ($[M+H]^+$), $C_{15}H_{13}O_2NSCl$ (306.04).

Sulfoxide-3-(4-chlorophenyl)-2-phenyl-1,3-thiazolidin-4-one (2e). Yield (98%); R_f = 0.094; m.p. 164-165 ^oC; IR: cm^{-1} 1715.7 (C=O), 1053.0 (S=O); ^1H NMR ($CDCl_3$): 7.42 – 7.21 (9 H, aromatics). Major isomer (96%), 5.88 (1H, s, C2), 3.82 (1H, d, C5, J = 17.0 Hz), 3.50 (1H, d, C5, J = 17.0 Hz). Minor isomer (4%), 5.97 (1H, s, C2), 3.92 (1H, d, C5, J = 16.7 Hz), 3.73 (1H, d, C5, J = 17.1 Hz); ^{13}C NMR: 168.44 (C4), 136.63, 132.47, 130.39, 130.31, 130.13, 129.55, 129.24, 129.12, 129.03, 126.34, 126.02, 125.74, 124.56, 121.09, 114.70, 86.26 (C2), 52.28 (C5); MS: (m/z) 306 ($[M+H]^+$), $C_{15}H_{13}O_2NSCl$ (306.04).

Sulfoxide-3-(3-fluorophenyl)-2-phenyl-1,3-thiazolidin-4-one (**2f**). Yield (99%); R_f = 0.137; m.p. 149-152 ^oC; IR: cm^{-1} 1709.5 (C=O), 1055.8 (S=O); ^1H NMR ($CDCl_3$): 7.46 – 6.85 (9 H, aromatics). Major isomer (93%), 6.01 (1H, s, C2), 3.86 (1H, d, C5, J = 17.4 Hz), 3.55 (1H, dd, C5, J = 1.6 Hz and J = 17.4 Hz). Minor isomer (7%), 6.07 (1H, s, C2), 3.98 (1H, d, C5, J = 16.8 Hz), 3.76 (1H, d, C5, J = 16.6 Hz); ^{13}C NMR: 168.60 (C4), 162.86 (d, J = 246.4), 139.55 (d, J = 12.8 Hz), 130.50 (d, J = 9.6 Hz), 130.21, 130.58, 128.96 (d, J = 12.8), 128.04, 126.26, 120.1 (J = 3.1 Hz), 118.15 (d, J = 2.3 Hz), 113.68 (d, J = 21.5 Hz), 112.29 (d, J = 25.9 Hz), 110.50 (d, J = 25.3 Hz), 85.98 (C2), 52.27 (C5); MS: (m/z) 290 ($[M+H]^+$), $C_{15}H_{13}O_2NSF$ (290.07).

Sulfoxide-3-(4-fluorophenyl)-2-phenyl-1,3-thiazolidin-4-one (**2g**). Yield (99%); R_f = 0.230; m.p. 188-190 ^oC; IR: cm^{-1} 1705.0 (C=O), 1046.8 (S=O); ^1H NMR ($CDCl_3$): 7.51 – 6.96 (9 H, aromatics). Major isomer (96%), 5.89 (1H, s, C2), 3.90 (1H, d, C5, J = 16.9 Hz), 3.58 (1H, dd, C5, J = 1.1 Hz and J = 17.0 Hz). Minor isomer (4%), 6.01 (1H, s, C2), 3.98 (1H, d, C5, J = 16.5 Hz), 3.81 (1H, d, C5, J = 16.7 Hz); ^{13}C NMR: 168.55 (C4), 161.28 (d, J = 231.2), 134.05 (d, J = 4.3 Hz), 130.64, 130.34, 130.17, 129.14 (d, J = 4.0 Hz), 126.76 (d, J = 8.5), 126.44, 125.79 (J = 9.6 Hz), 116.45 (d, J = 25.5 Hz), 86.82 (C2), 52.27 (C5); MS: (m/z) 290 ($[M+H]^+$), $C_{15}H_{13}O_2NSF$ (290.07).

Sulfoxide-3-(3-bromophenyl)-2-phenyl-1,3-thiazolidin-4-one (**2h**). Yield (75%); R_f = 0.112; m.p. 167-169 ^oC; IR: cm^{-1} 1683.9 (C=O), 1052.8 (S=O); ^1H NMR ($CDCl_3$): 7.64 – 7.04 (9 H, aromatics). Major isomer (94%), 5.92 (1H, s, C2), 3.80 (1H, d, C5, J = 16.9 Hz), 3.49 (1H, dd, C5, J = 1.2 Hz and J = 17.0 Hz). Minor isomer (6%), 6.00 (1H, s, C2), 3.92 (1H, d, C5, J = 16.7 Hz), 3.70 (1H, d, C5, J = 16.5 Hz); ^{13}C NMR: 168.47 (C4), 139.29, 130.53, 130.18, 130.02, 129.91, 128.96, 128.93, 126.23, 122.79, 121.52, 85.91 (C2), 52.17 (C5); MS: (m/z) 350 ($[M+H]^+$), $C_{15}H_{13}O_2NSBr$ (349.99).

Sulfoxide-3-(4-bromophenyl)-2-phenyl-1,3-thiazolidin-4-one (**2i**). Yield (99%); R_f = 0.134; m.p. 190-191 ^oC; IR: cm^{-1} 1715.0 (C=O), 1048.5 (S=O); ^1H NMR ($CDCl_3$): 7.46 – 7.09 (9 H, aromatics). Major isomer (89%), 5.91 (1H, s, C2), 3.84 (1H, d, C5, J = 17.3 Hz), 3.54 (1H, dd, C5, J = 1.3 Hz and J = 17.0 Hz). Minor isomer (11%), 5.95 (1H, s, C2), 3.95 (1H, d, C5, J = 16.7 Hz), 3.77 (1H, d, C5, J = 16.7 Hz); ^{13}C NMR: 168.42 (C4), 137.18, 132.54, 132.23, 130.43, 130.39, 130.34, 130.17, 129.17, 129.02, 126.34, 124.81, 120.37, 86.23 (C2), 53.79 (C5), 52.17 (C5); MS: (m/z) 350 ($[M+H]^+$), $C_{15}H_{13}O_2NSBr$ (349.99).

Sulfoxide-3-(3-methylphenyl)-2-phenyl-1,3-thiazolidin-4-one (**2j**). Yield (97%); R_f = 0.143; m.p. 161-162 ^oC; IR: cm^{-1} 1678.2 (C=O), 1048.4 (S=O); ^1H NMR ($CDCl_3$): 7.42 – 6.98 (9 H, aromatics). Major isomer (96%), 5.95 (1H, s, C2), 3.86 (1H, d, C5, J = 17.0 Hz), 3.57 (1H, dd, C5, J = 1.1 Hz and J = 17.0 Hz). Minor isomer (4%), 6.06 (1H, s, C2), 3.95 (1H, d, C5, J = 16.7 Hz), 3.70 (1H, d, C5, J = 16.5 Hz), 2.24 (3 H, s); ^{13}C NMR: 168.43 (C4), 139.38, 137.81,

130.67, 129.93, 129.82, 129.09, 128.71, 127.94, 126.35, 124.71, 124.44, 120.68, 120.45, 116.91, 86.46 (C2), 52.19 (C5), 21.41 (CH_3); MS: (m/z) 286 ($[M+H]^+$), $C_{16}H_{16}O_2NS$ (286.09).

Sulfoxide-3-(4-methylphenyl)-2-phenyl-1,3-thiazolidin-4-one (**2k**). Yield (97%); R_f = 0.157; m.p. 179-180 ^oC; IR: cm^{-1} 1704.9 (C=O), 1051.1 (S=O); ^1H NMR ($CDCl_3$): 7.44 – 6.96 (9H, aromatics), 5.91 (1H, s, C2), 4.04 (1H, d, C5, J = 16.7 Hz), 3.99 (1H, d, C5, J = 16.7 Hz), 2.29 (3 H, s); ^{13}C NMR: 168.34 (C4), 137.02, 135.32, 130.80, 129.93 (br), 129.84, 126.41, 123.66, 86.57 (C2), 52.24 (C5), 21.01 (CH_3); MS: (m/z) 286 ($[M+H]^+$), $C_{16}H_{16}O_2NS$ (286.09).

Sulfoxide-3-(3-methoxyphenyl)-2-phenyl-1,3-thiazolidin-4-one (**2l**). Yield (99%); R_f = 0.056; m.p. d 219 ^oC; IR: cm^{-1} 1693.2 (C=O), 1027.7 (S=O); ^1H NMR ($CDCl_3$): 7.55 – 6.66 (9H, aromatics). Major isomer (91%), 5.46 (1H, s, C2), 3.62 (2H, s, C5). Minor isomer (9%), 5.64 (1H, s, C2), 3.80 (1H, d, C5, J = 1.7 Hz), 3.78 (3 H and minor isomer's C5, s); ^{13}C NMR: 165.96 (C4), 138.17, 133.46, 131.56, 131.18, 130.51, 130.26, 129.59, 129.34, 129.17, 129.01, 122.40, 112.63, 110.10, 71.45 (C2), 55.84 (OCH_3), 52.19 (C5); MS: (m/z) 302 ($[M+H]^+$), $C_{16}H_{16}O_3NS$ (302.09).

Sulfoxide-3-(4-methoxyphenyl)-2-phenyl-1,3-thiazolidin-4-one (**2m**). Yield (99%); R_f = 0.101; m.p. 188-189 ^oC; IR: cm^{-1} 1697.7 (C=O), 1049.4, 1027.2 (S=O); ^1H NMR ($CDCl_3$): 7.49 – 6.84 (9 H, aromatics). Major isomer (93%), 5.86 (1H, s, C2), 3.91 (1H, d, C5, J = 17.2 Hz), 3.56 (1H, dd, J = 0.9 Hz and J = 17.2 Hz). Minor isomer (7%), 5.99 (1H, s, C2), 3.97 (1H, d, C5, J = 16.3 Hz), 3.76 (3 H and minor isomer's C5, s); ^{13}C NMR: 168.49 (C4), 158.65, 130.97, 130.66, 130.16, 130.04, 129.13, 129.03, 126.54, 126.38, 125.80, 114.68, 114.49, 87.16 (C2), 55.63 (OCH_3), 52.31 (C5); MS: (m/z) 302 ($[M+H]^+$), $C_{16}H_{16}O_3NS$ (302.09).

Sulfoxide-3-(3-nitrophenyl)-2-phenyl-1,3-thiazolidin-4-one (**2n**). Yield (99%); R_f = 0.089; m.p. 205-207 ^oC; IR: cm^{-1} 1702.9 (C=O), 1062.4 (br, S=O); ^1H NMR ($CDCl_3$): 8.28 – 7.19 (9 H, aromatics). Major isomer (90%), 5.97 (1H, s, C2), 3.86 (1H, d, C5, J = 17.0 Hz), 3.58 (1H, dd, J = 1.2 Hz and J = 17.1 Hz). Minor isomer (10%), 6.05 (1H, s, C2), 3.96 (1H, d, C5, J = 17.1 Hz), 3.84 (1H, d, J = 17.1 Hz); ^{13}C NMR: 168.73 (C4), 148.83, 139.41, 130.74, 130.49, 130.40, 129.83, 129.48, 129.17, 128.49, 126.26, 121.63, 121.52, 117.79, 86.03 (C2), 52.38 (C5); MS: (m/z) 317 ($[M+H]^+$), $C_{15}H_{13}O_4N_2S$ (317.06).

Sulfoxide-3-(4-nitrophenyl)-2-phenyl-1,3-thiazolidin-4-one (**2o**). Yield (44%); R_f = 0.075; m.p. d 213 ^oC; IR: cm^{-1} 1706.2 (C=O), 1051.4 (br, S=O); ^1H NMR ($CDCl_3$): 8.22 – 7.35 (9 H, aromatics), 6.08 (1H, s, C2), 3.90 (1H, d, C5, J = 17.4 Hz), 3.65 (1H, dd, J = 1.2 Hz and J = 17.3 Hz); ^{13}C NMR: 168.83 (C4), 145.16, 143.92, 130.71, 130.47, 129.68, 126.16, 125.00, 122.07, 85.64 (C2), 52.41 (C5); MS: (m/z) 317 ($[M+H]^+$), $C_{15}H_{13}O_4N_2S$ (317.06).

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 **3m** 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-2-phenyl-2-(3-trifluoromethylphenyl)-1,3-thiazolidin-4-one (**3a**). Yield: (78%); R_f = 0.219; m.p. 106-110 ^oC; IR cm^{-1} 1702.6 (C=O), 1126.2, 1114.1 (S=O); ^1H NMR ($CDCl_3$), 7.71 – 7.33 (9 H, aromatics), 6.13 (1H, s, C2), 4.16 (1H, d, C5, J = 17.1 Hz), 4.12 (1H, d, C5, J = 17.1 Hz); ^{13}C NMR: 162.72 (C4), 131.84 (q, J = 33.1), 131.05, 130.23, 130.08, 129.7, 128.61, 128.22, 123.43 (q, J = 272.4 Hz), 124.51 (br q, J = 3.2 Hz), 121.93 (br q, J = 3.9 Hz), 83.22 (C2), 50.67 (C5); MS: (m/z) 356 ($[M+H]^+$), $C_{16}H_{13}O_3NSF_3$ (356.06).

Sulfone-2-phenyl-2-(4-trifluoromethylphenyl)-1,3-thiazolidin-4-one (**3b**). Yield: (81%); m.p. 186-187 ^oC; IR cm^{-1} 1697.8 (C=O), 1123.1 (S=O); ^1H NMR ($CDCl_3$), 7.60 – 7.36 (9 H, aromatics), 6.01 (1H, s, C2), 4.09 (1H, d, C5, J = 16.6 Hz), 4.04 (1H, d, C5, J = 16.6 Hz); ^{13}C NMR: 162.62 (C4), 139.33, 129.88, 129.78, 129.61 (q, J = 32.4 Hz), 128.43, 127.90, 126.69 (q, J = 4.2 Hz), 124.76, 123.64 (q, J = 272.1 Hz), 83.23 (C2), 50.69 (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 (**3c**). Yield (76%); R_f = 0.366; m.p. 178-180 ^oC: IR: cm^{-1} 1693.1 (C=O), 1141.6, 1125.2 (S=O); ^1H 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-3-(3-chlorophenyl)-2-phenyl-1,3-thiazolidin-4-one (3d). Yield (82%); m.p. 183-184 ^oC; IR: cm^{-1} 1694.8 (C=O), 1130.4 (S=O); ^1H NMR ($CDCl_3$): 7.47 – 7.13 (9 H, aromatics), 5.92 (1H, s, C2), 4.04 (1H, d, C5, J = 16.7 Hz), 4.00 (1H, d, C5, J = 16.7 Hz); ^{13}C NMR: 162.51 (C4), 137.31, 135.19, 131.11, 130.51, 129.82, 128.62, 128.24, 127.93, 125.34, 122.98, 83.62 (C2), 50.64 (C5); MS: (m/z) 322 ($[M+H]^+$), $C_{15}H_{13}O_3NSCl$ (322.03).

Sulfone-3-(4-chlorophenyl)-2-phenyl-1,3-thiazolidin-4-one (3e). Yield (76%); m.p. 176-178 ^{o}C; IR: cm^{-1} 1702.9 (C=O), 1129.3, 1089.6 (S=O); ^{1}H NMR ($CDCl_3$): 7.41 – 7.16 (9 H, aromatics), 5.87 (1H, s, C2), 4.00 (1H, d, C5, J = 16.8 Hz), 3.96 (1H, d, C5, J = 16.3 Hz); ^{13}C NMR: 162.54 (C4), 134.68, 133.87, 131.10, 129.78, 129.76, 128.56, 128.06, 126.33, 83.66 (C2), 50.71 (C5); MS: (m/z) 322 ($[M+H]^+$), $C_{15}H_{13}O_3NSCl$ (322.03).

Sulfone-3-(3-fluorophenyl)-2-phenyl-1,3-thiazolidin-4-one (**3f**). Yield (77%); m.p. 171-172 ^{o}C; IR: cm^{-1} 1707.3 (C=O), 1058.8 (S=O); ^{1}H NMR ($CDCl_3$): 7.42 – 6.88 (9 H, aromatics), 5.90 (1H, s, C2), 3.99 (2H, overlapping d, C5, J = 17.5 Hz); ^{13}C NMR: 162.81 (d, J = 246.3), 162.53 (C4), 137.61 (d, J = 9.7 Hz), 131.06, 130.74 (d, J = 9.6 Hz), 129.80, 128.69, 127.90, 120.23 (d, J = 2.4), 112.61 (d, J = 25.2 Hz), 83.54 (C2), 50.70 (C5); MS: (m/z) 306 ($[M+H]^+$), $C_{15}H_{13}O_3NSF$ (306.06).

Sulfone-3-(4-fluorophenyl)-2-phenyl-1,3-thiazolidin-4-one (**3g**). Yield (56%); m.p. 141-142 ^{o}C; IR: cm^{-1} 1699.0 (C=O), 1142.0, 1122.5 (S=O); ^{1}H NMR ($CDCl_3$): 7.45 – 6.96 (9 H, aromatics), 5.91 (1H, s, C2), 4.04 (1H, d, C5, J = 16.7 Hz), 3.99 (1H, d, C5, J = 16.8 Hz); ^{13}C NMR: 162.83 (C4), 161.52 (d, J = 236.1), 132.05 (d, J = 3.5 Hz), 131.00, 129.67, 128.62, 128.16, 127.25 (d, J = 9.4 Hz), 116.57 (d, J = 22.5 Hz), 83.93 (C2), 50.64 (C5); MS: (m/z) 306 ($[M+H]^+$), $C_{15}H_{13}O_3NSF$ (306.06).

Sulfone-3-(3-bromophenyl)-2-phenyl-1,3-thiazolidin-4-one (**3h**). Yield (77%); m.p. 190-191 ^{o}C; IR: cm^{-1} 1693.8

(C=O), 1128.1 (S=O); ^{1}H NMR ($CDCl_3$): 7.55 – 7.17 (9 H, aromatics), 5.94 (1H, s, C2), 4.06 (1H, d, C5, J = 16.7 Hz), 4.02 (1H, d, C5, J = 16.7 Hz); ^{13}C NMR: 162.51 (C4), 137.43, 131.19, 131.12, 130.77, 129.84, 128.62, 128.21, 127.94, 123.50, 123.00, 83.66 (C2), 50.64 (C5); MS: (m/z) 366 ($[M+H]^+$), $C_{15}H_{13}O_3NSBr$ (365.98).

Sulfone-3-(4-bromophenyl)-2-phenyl-1,3-thiazolidin-4-one (**3i**). Yield (76%); m.p. 201-204 ^{o}C; IR: cm^{-1} 1698.8 (C=O), 1128.6 (S=O); ^{1}H NMR ($CDCl_3$): 7.49 – 7.16 (9 H, aromatics), 5.93 (1H, s, C2), 4.07 (1H, d, C5, J = 16.7 Hz), 4.02 (1H, d, C5, J = 16.8 Hz); ^{13}C NMR: 162.46 (C4), 135.24, 132.74, 131.12, 129.81, 128.57, 128.03, 126.56, 121.63, 83.62 (C2), 50.73 (C5); MS: (m/z) 366 ($[M+H]^+$), $C_{15}H_{13}O_3NSBr$ (365.98).

Sulfone-3-(3-methylphenyl)-2-phenyl-1,3-thiazolidin-4-one (**3j**). Yield (65%); m.p. 173-175 ^{o}C; IR: cm^{-1} 1687.2 (C=O), 1138.5, 1124.0 (S=O); ^{1}H NMR ($CDCl_3$): 7.47 – 7.03 (9H, aromatics), 5.95 (1H, s, C2), 4.05 (1H, d, C5, J = 16.5 Hz), 4.00 (1H, d, C5, J = 16.5 Hz), 2.30 (3H, s); ^{13}C NMR: 162.60 (C4), 139.75, 136.16, 130.84, 129.62, 129.37, 129.20, 129.04, 128.00, 125.97, 122.22, 84.14 (C2), 50.68 (C5), 21.55 (CH_3); MS: (m/z) 302 ($[M+H]^+$), $C_{16}H_{16}O_3NS$ (302.09).

Sulfone-3-(4-methylphenyl)-2-phenyl-1,3-thiazolidin-4-one (**3k**). Yield (78%); m.p. 104-105 ^{o}C; IR: cm^{-1} 1701.9 (C=O), 1128.0 (S=O); ^{1}H NMR ($CDCl_3$): 7.45 – 7.11 (9H, aromatics), 5.95 (1H, s, C2), 4.05 (1H, d, C5, J = 16.7 Hz), 4.00 (1H, d, C5, J = 16.6 Hz), 2.29 (3 H, s); ^{13}C NMR: 162.58 (C4), 138.18, 133.55, 130.80, 130.17, 129.56, 129.05, 128.12, 125.12, 84.05 (C2), 50.71 (C5), 21.20 (CH_3); MS: (m/z) 302 ($[M+H]^+$), $C_{16}H_{16}O_3NS$ (302.09).

Sulfone-3-(3-methoxyphenyl)-2-phenyl-1,3-thiazolidin-4-one (**3l**). Yield (83%); m.p. 214-217 ^{o}C; IR: cm^{-1} 1689.3 (C=O), 1129.1, 1107.4 (S=O); ^{1}H NMR ($CDCl_3$): 7.46 – 6.82 (9H, aromatics), 5.64 (1H, s, C2,), 4.16 (1H, d, C5, J = 12.7 Hz), 3.97 (1H, dd, C5, J = 1.7 Hz and J = 12.7 Hz), 3.82 (3H, s); ^{13}C NMR: 161.07 (C4), 137.27, 131.58, 131.51, 129.81, 129.31, 128.54, 120.38, 114.29, 109.87, 69.07 (C2), 55.90; MS: (m/z) 318 ($[M+H]^+$), $C_{16}H_{16}O_4NS$ (318.08).

Sulfone-3-(4-methoxyphenyl)-2-phenyl-1,3-thiazolidin-4-one (**3m**). Yield (95%); R_f = 0.265; m.p. 104-105 ^{o}C; IR: cm^{-1} 1694.1 (C=O), 1126.8 (S=O); ^{1}H NMR ($CDCl_3$): 7.44 – 6.81 (9 H, aromatics), 5.95 (1H, s, C2), 4.04 (1H, d, C5, J = 17.1 Hz), 3.99 (1H, d, J = 16.4 Hz), 3.73 (3H, s); ^{13}C NMR: 162.76 (C4), 158.93, 130.71, 129.44, 128.86, 128.66, 128.25, 126.85, 114.67, 84.06 (C2), 55.51 (OCH_3), 50.63 (C5); MS: (m/z) 318 ($[M+H]^+$), $C_{16}H_{16}O_4NS$ (318.08).

Sulfone-3-(3-nitrophenyl)-2-phenyl-1,3-thiazolidin-4-one (**3n**). Yield (80%); m.p. 199-201 ^{o}C; IR: cm^{-1} 1698.0 (C=O), 1132.0 (S=O); ^{1}H NMR ($CDCl_3$): 8.21 – 7.37 (9H, aromatics), 6.04 (1H, s, C2), 4.11 (2H, s); ^{13}C NMR: 162.63 (C4), 148.71, 137.25, 131.41, 130.50, 130.45, 130.04, 128.04, 127.88, 122.51, 119.79, 83.20 (C2), 50.74 (C5); MS: (m/z) 333 ($[M+H]^+$), $C_{15}H_{13}O_5N_2S$ (333.05).

Sulfone-3-(4-nitrophenyl)-2-phenyl-1,3-thiazolidin-4-one (**3o**). Yield (56%); m.p. 204-206 ^{o}C; IR: cm^{-1} 1709.4 (C=O), 1125.7, 1111.7 (S=O); ^{1}H NMR ($CDCl_3$): 8.17 – 7.35 (9 H, aromatics), 6.07 (1H, s, C2), 4.10 (2H, s); ^{13}C NMR: 162.66 (C4), 145.86, 141.72, 131.34, 129.97, 127.90, 127.86, 124.86, 124.56, 82.72 (C2), 52.41 (C5); MS: (m/z) 333 ($[M+H]^+$), $C_{15}H_{13}O_4N_2S$ (333.05).

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

Thiazolidin-4-one (**1a-o)** (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, 201**7**). 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 ratio of sulfoxide **2** to sulfone **3** was 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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