Synthesis of a New Class of Arylsulfonylethylsulfonylmethyloxazolines and Thiazolines

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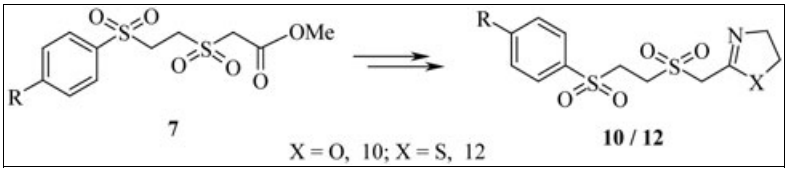

A new class of arylsulfonylethylsulfonylmethyl oxazolines and thiazolines were prepared using multistep, one-pot methodologies exploiting lanthanide alkoxides and under microwave irradiation. The microwave method provides an excellent approach in a single step with high yields.

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INTRODUCTION

Oxazolines and thiazolines are important constituents of numerous bioactive natural products of peptide origin. Their wide range of antitumor, antiviral, and antibiotic activities has fueled numerous synthetic investigations [1]. In addition, 2-oxazolines are excellent catalyst ligands [2–4], protecting groups [5], and monomers for the cationic ring-opening polymerization [6–10]. Thiazoles are important building blocks for preparing various pharmaceuticals. Recently, many natural products containing thiazole moiety were isolated and most of them exhibit considerable cytotoxicities and antitumor potentials [11]. Though a number of 2-substituted oxazolines and thiazolines are commercially available, the modular synthesis of oxazolines and thiazolines containing a wide range of functional side chains would be advantageous for both biomedical and materials science applications. A variety of methods have been reported for the synthesis of oxazolines *viz.*, cyclodehydration of amidoalcohols [12], cyclocondensation of carboxylic acids [13], orthoesters [14], imidatehydrochlorides [15], imino ether hydrochlorides [16], and nitriles [17] with aminoalcohols[18]. Similarly, thiazolines are prepared by the coupling of imidates and esters with aminothiols [19], cyclodehydration of hydroxy thioamides [20], and heterocyclic interconversions from oxazolines [21] or oxazolidines [22]. Earlier, we have reported the synthesis of 2-oxazolines and 2-thiazolines from arylsulfonylacetic acid methyl ester, arylmethanesulfonylacetic acid methyl ester [23], and phenacylsulfonylacetic acid methyl ester [24]. In continuation of our interest, we, herein, report the synthesis of a new class of oxazolines and thiazolines from 2-(2-(arylsulfonyl) ethylsulfonyl)acetic acid (**6**).

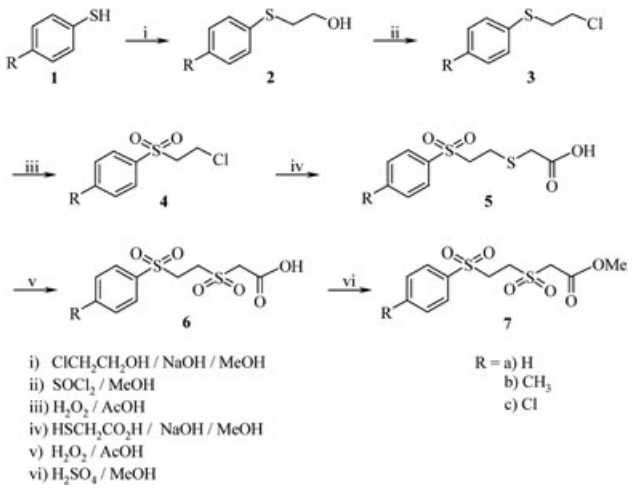
RESULTS AND DISCUSSION

The present communication deals with the synthesis of oxazolines and thiazolines by traditional four-step three intermediate route, one-pot methodology exploiting lanthanide alkoxides and microwave irradiation. The reactive intermediate 2-(2-(arylsulfonyl)ethyl-sulfonyl)acetic acid (**6**) was prepared as follows. The reaction of thiophenol (**1**) with 2-chloroethanol followed by chlorination and oxidation provided arylsulfonyl ethyl chloride (**4**). The reaction of **4** with 2-mercaptoacetic acid gave 2-(2-(arylsulfonyl) ethylthio)acetic acid (**5**), which on oxidation resulted in **6**. Esterification of **6** produced methyl 2-(2-(arylsulfonyl) ethyl-sulfonyl)acetate (**7**; Scheme 1).

The ester functionality in **7** was used to develop oxazoline and thiazoline rings by multistep methodology. The reaction of **7** with 2-aminoethanol provided *N*-(2-hydroxyethyl)-2-(arylsulfonylethylsulfonyl)acetamide (**8**). Chlorination of **8** with thionyl chloride furnished *N*-(2-chloroethyl)-2-(arylsulfonylethylsulfonyl)acetamide (**9**). Cyclocondensation of **9** with NaH afforded 2-((2-(arylsulfonyl)ethylsulfonyl)methyl)-4,5-dihydrooxazole (**10**; Scheme 2). In a similar way, the reaction of **7** with 2-aminoethanethiol gave *S*-2-aminoethyl 2-(2-(arylsulfonyl)-ethylsulfonyl)ethanethioate (**11**), which in the presence of NaH in THF produced 2-((2-(arylsulfonyl) ethylsulfonyl) methyl)-4,5-dihydrothiazole (**12**; Scheme 2, Method A).

Samarium chemistry was also exploited to prepare the compounds **10** and **12** in one-pot methodology. Thus, the reaction of **7** with 2-aminoethanol in the presence of *n*-butyllithium complexed with 5–10% molar equivalent of anhydrous samarium (III) chloride suspension in toluene gave **10**. Likewise, the compound **12** was obtained by

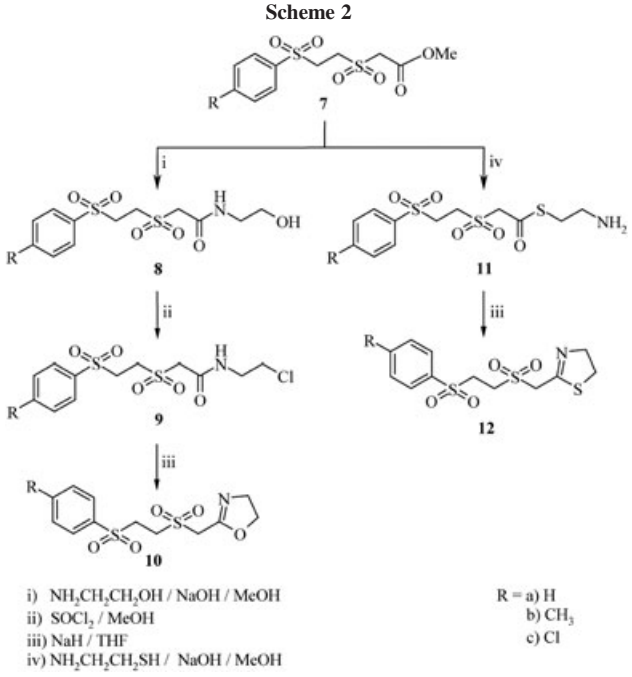
Scheme 1



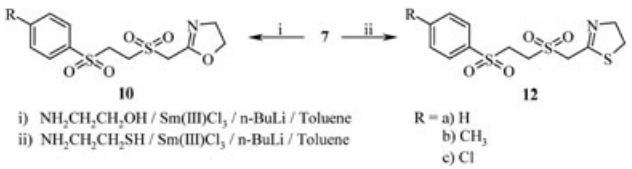
the reaction of **7** with aminoethanethiol in the presence of samarium chloride and *n*-butyllithium (Scheme 3; Method B).

The microwave assisted synthesis of compounds **10** and **12** was also carried out to establish the general validity of this technique for the development of oxazolines and thiazolines. The direct irradiation of compound **6** and 2-aminoethanol at 540 watts for 3–5 min gave the compound **10**. Similarly, the microwave irradiation of compound **6** with 2-aminoethanethiol at 560 watts for 4–5 min resulted in **12** (Scheme 4; Method C). The products **10** and **12** were isolated by solvent extraction and purified by

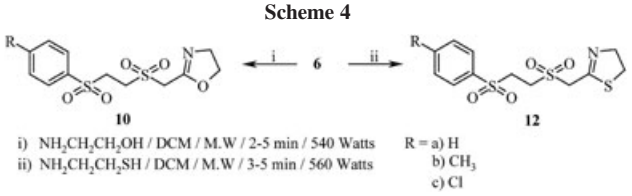
Scheme 2



Scheme 3



Scheme 4



column chromatography. The structures of all the compounds **6–12** are ascertained by ^1H and ^{13}C NMR spectra. (See Tables 1–3.)

CONCLUSIONS

A new class of arylsulfonylethylsulfonylmethyl oxazolines and thiazolines were synthesized from the synthetically vulnerable intermediate 2-(2-(arylsulfonyl) ethylsulfonyl)-acetic acid by traditional four-step three intermediate routes, one-pot methodologies using samarium (III) chloride and under microwave irradiation. The microwave methodology provides an excellent approach in a single step with high yields.

EXPERIMENTAL

Melting points were determined in open capillaries on a Mel–Temp apparatus and are uncorrected. The purity of the compounds was checked by TLC (silica gel H, BDH, hexane/ethyl acetate, 3:1). The IR spectra were recorded on a Thermo Nicolet IR 200 FTIR spectrometer as KBr pellets, and the wave numbers were given in cm^{-1}. The ^1H NMR spectra were recorded in $CDCl_3$/DMSO-d_6 on a Jeol JNM λ-400 MHz. The ^{13}C NMR spectra were recorded in $CDCl_3$/DMSO-d_6 on a Jeol JNM spectrometer operating at λ-100 MHz. All chemical shifts are reported in ppm using TMS as an internal standard. The microanalyses were performed on a Perkin–Elmer 240C elemental analyzer.

Multistep synthesis of 2-oxazolines and 2-thiazolines. ***Methyl 2-(2-(arylsulfonyl)ethylsulfonyl)acetate (7).*** *General procedure.* A solution of 2-(2-(arylsulfonyl)ethylsulfonyl) acetic acid (**6**; 10 mmol) in methanol (10 mL) and Conc. H_2SO_4 (1 mL) was refluxed on a steam bath for 4–5 h. The contents of the flask were cooled and poured onto crushed ice. The solid separated was collected by filtration, washed with cold water, and dried. The crude product was recrystallized from methanol to get pure methyl 2-(2-(phenylsulfonyl) ethylsulfonyl)acetate (**7a**; 68%), mp 121–123 °C; methyl 2-(2-tosylethylsulfonyl)acetate (**7b**; 70%), mp 142–144 °C; and methyl 2-(2-(4-chlorophenyl-sulfonyl)ethylsulfonyl)acetate (**7c**; 72%), mp 157–159 °C.

Table 1

Physical data and analytical data for compounds **10** and **12**.

Compd. No.	Mp (°C)	Yield (%)	Molecular formula	Analyses % Calcd. (Found)		
				C	H	N
10a	153–155	70, 75,[a] 95[b]	$C_{12}H_{15}NO_5S_2$	45.41–45.48	4.76–4.78	4.41–4.47
10b	135–137	72, 78,[a] 92[b]	$C_{13}H_{17}NO_5S_2$	47.11–47.16	5.17–5.13	4.23–4.27
10c	166–168	75, 80,[a] 94[b]	$C_{12}H_{14}ClNO_5S_2$	40.97–41.01	4.01–4.02	3.98–4.04
12a	157–159	69, 73,[a] 94[b]	$C_{12}H_{15}NO_4S_3$	43.22–43.29	4.53–4.50	4.20–4.25
12b	150–152	68, 76,[a] 90[b]	$C_{13}H_{17}NO_4S_3$	44.94–44.98	4.93–4.95	4.03–4.07
12c	178–180	69, 72,[a] 93[b]	$C_{12}H_{14}ClNO_4S_3$	39.18–39.15	3.84–3.89	3.81–3.86

[a]Yields in Method B.
[b]Yields in Method C.

Table 2

IR data of compounds **7–12**.

Compounds	IR (KBr) (cm^{-1})						
	SO_2		C = N	C = O	NH	OH	NH_2
7a	1143	1336	–	1735	–	–	–
7b	1138	1330	–	1729	–	–	–
7c	1132	1328	–	1730	–	–	–
8a	1141	1325	–	1645	3334	3390	–
8b	1136	1330	–	1639	3343	3381	–
8c	1139	1337	–	1643	3338	3375	–
9a	1137	1330	–	658	3340	–	–
9b	1134	1324	–	1670	3324	–	–
9c	1140	1335	–	1664	3335	–	–
10a	1129	1332	1575	–	–	–	–
10b	1135	1340	1584	–	–	–	–
10c	1129	1329	1570	–	–	–	–
11a	1130	1341	–	1650	–	–	3410, 3325
11b	1126	1339	–	1645	–	–	3420, 3330
11c	1134	1333	–	1647	–	–	3415, 3310
12a	1137	1330	1560	–	–	–	–
12b	1138	1338	1550	–	–	–	–
12c	1135	1345	1565	–	–	–	–

N-(2-Hydroxyethyl)-2-(arylsulfonylethylsulfonyl)acetamide (8). *General Procedure.* A mixture of methyl 2-(2-(arylsulfonyl) ethylsulfonyl)acetate (**7**; 10 mmol), 2-aminoethanol (10 mmol), methanol (5 mL), and NaOMe (10 mmol) was refluxed for 6–8 h. The solution was concentrated, cooled, and poured onto crushed ice. The solid separated was filtered, dried, and recrystallized from methanol yielded analytically pure *N*-(2-hydroxyethyl)-2-(phenylsulfonylethylsulfonyl)acetamide (**8a**; 70%), mp 100–102 °C; *N*-(2-hydroxyethyl)-2-(4-methylphenyl-sulfonylethylsulfonyl)acetamide (**8b**; 74%), mp 115–117 °C; and *N*-(2-hydroxyethyl)-2-(4-chlorophenylsulfonylethylsulfonyl) acetamide (**8c**; 72%), mp 132–134 °C.

N-(2-Chloroethyl)-2-(arylsulfonylethylsulfonyl)acetamide (9). *General Procedure.* The compound *N*-(2-hydroxyethyl)-2-(arylsulfonylethylsulfonyl)acetamide (**8**; 10 mmol), thionyl chloride (15 mmol), and methanol (10 mL) were refluxed for 11–13 h. It was cooled and poured onto crushed ice. The solid separated was filtered, dried, and crystallized from methanol to get pure *N*-(2-chloroethyl)-2-(phenylsulfonylethylsulfonyl) acetamide (**9a**; 65%), mp 151–153 °C; *N*-(2-chloroethyl)-2-(4-methylphenylsulfonylethylsulfonyl)acetamide (**9b**; 68%), mp 142–144 °C; and *N*-(2-chloroethyl)-2-(4-chlorophenylsulfonyle-thylsulfonyl)-acetamide (**9c**; 71%), mp 170–172 °C.

2-((2-(Arylsulfonyl)ethylsulfonyl)methyl)-4,5-dihydrooxazole (10). *General Procedure.* To a solution of *N*-(2-chloroethyl)-2-(arylsulfonylethylsulfonyl)acetamide (**9**; 1 mmol) in tetrahydrofuran (3 mL), a catalytic amount of sodium hydride was added and refluxed for 4–7 h. The reaction mixture was allowed to attain room temperature and poured onto crushed ice. The solid obtained was filtered, dried, and recrystallized from methanol.

S-2-Aminoethyl 2-(2-(arylsulfonyl)ethylsulfonyl)ethanethioate (11). *General Procedure.* A mixture of methyl 2-(2-(arylsulfonyl) ethylsulfonyl)acetate (**7**; 1 mmol), 2-aminoethanethiol (1.5 mmol), methanol (5 mL), and NaOMe (1 mmol) was refluxed for 3–5 h. The solution was cooled and poured onto crushed ice. The solid separated was filtered, dried, and recrystallized from methanol to

Table 3

3^{1}H and ^{13}C NMR data of compounds **6–12**.

Compound	^{1}H NMR (δ, ppm)	^{13}C NMR (δ, ppm)
6a	3.33 (t, 2H, CH_2—SO_2, J = 4.2 Hz), 3.40 (t, 2H, SO_2—CH_2, J = 4.2 Hz), 4.42 (s, 2H, CH_2—CO), 7.68–8.03 (m, 5H, Ar-H), 13.58 (bs, 1H, OH)	46.8 (CH_2—SO_2), 48.1 (SO_2—CH_2), 57.5 (*C*H_2—CO), 164.9 (CO), 128.4, 130.1, 134.9, 138.4 (aromatic carbons)
6b	2.35 (s, 3H, Ar-CH_3), 3.39 (t, 2H, CH_2—SO_2, J = 4.0 Hz), 3.46 (t, 2H, SO_2—CH_2, J = 4.0 Hz), 4.49 (s, 2H, CH_2—CO), 7.71–8.05 (m, 4H, Ar-H), 12.71 (bs, 1H, OH)	23.8 (Ar-CH_3), 45.6 (CH_2—SO_2), 47.2 (SO_2—CH_2), 58.7 (*C*H_2—CO), 165.2 (CO), 129.2, 131.7, 133.6, 139.5 (aromatic carbons)
6c	3.29 (t, 2H, CH_2—SO_2, J = 4.3 Hz), 3.41 (t, 2H, SO_2—CH_2, J = 4.3 Hz), 4.40 (s, 2H, CH_2—CO), 7.52–7.98 (m, 4H, Ar-H), 12.91 (bs, 1H, OH)	46.1 (CH_2—SO_2), 47.9 (SO_2—CH_2), 56.9 (*C*H_2—CO), 163.7 (CO), 128.9, 131.4, 134.1, 137.2 (aromatic carbons)
7a	3.58 (t, 2H, CH_2—SO_2, J = 4.0 Hz), 3.68 (t, 2H, SO_2—CH_2, J = 4.0 Hz), 3.82 (s, 3H, OCH_3), 4.05 (s, 2H, CH_2—CO), 7.60–7.95 (m, 5H, Ar-H)	46.9 (CH_2—SO_2), 48.6 (SO_2—CH_2), 53.3 (OCH_3), 57.9 (*C*H_2—CO), 162.8 (CO), 128.1, 129.5, 134.3, 138.2 (aromatic carbons)
7b	2.41 (s, 3H, Ar-CH_3), 3.49 (t, 2H, CH_2—SO_2, J = 4.2 Hz), 3.61 (t, 2H, SO_2—CH_2, J = 4.2 Hz), 3.79 (s, 3H, OCH_3), 4.13 (s, 2H, CH_2—CO), 7.66–8.01 (m, 4H, Ar-H)	24.9 (Ar-CH_3), 45.4 (CH_2—SO_2), 47.6 (SO_2—CH_2), 54.1 (OCH_3), 58.6 (*C*H_2—CO), 164.7 (CO), 130.1, 132.0, 134.7, 139.5 (aromatic carbons)
7c	3.50 (t, 2H, CH_2—SO_2, J = 4.3 Hz), 3.59 (t, 2H, SO_2—CH_2, J = 4.3 Hz), 3.80 (s, 3H, OCH_3), 4.12 (s, 2H, CH_2—CO), 7.58–8.01 (m, 4H, Ar-H)	45.7 (CH_2—SO_2), 47.9 (SO_2—CH_2), 53.8 (OCH_3), 56.4 (*C*H_2—CO), 164.2 (CO), 129.2, 130.5, 134.7, 137.1 (aromatic carbons)
8a	3.12 (t, 2H, NH—C*H*$_2$, J = 4.2 Hz), 3.34 (t, 2H, C*H*$_2$—OH, J = 4.2 Hz), 3.60 (t, 2H, CH_2—SO_2, J = 4.8 Hz), 3.73 (t, 2H, SO_2—CH_2, J = 4.8 Hz), 4.22 (s, 2H, CH_2—CO), 4.75 (bs, 1H, OH), 7.69–7.94 (m, 5H, Ar-H), 8.39 (bs, 1H, NH)	42.2 (NH—CH_2), 47.0 (CH_2—SO_2), 48.2 (SO_2—CH_2), 58.2 (*C*H_2—CO), 59.8 (CH_2—OH), 162.1 (CO-NH), 128.4, 130.1, 134.9, 138.4 (aromatic carbons)
8b	2.32 (s, 3H, Ar-CH_3), 3.24 (t, 2H, NH—C*H*$_2$, J = 4.3 Hz), 3.38 (t, 2H, C*H*$_2$—OH, J = 4.3 Hz), 3.56 (t, 2H, CH_2—SO_2, J = 5.0 Hz), 3.69 (t, 2H, SO_2—CH_2, J = 5.0 Hz), 4.34 (s, 2H, CH_2—CO), 4.81 (bs, 1H, OH), 7.60–8.03 (m, 4H, Ar-H), 8.51 (bs, 1H, NH)	22.9 (ar-CH_3), 43.4 (NH—CH_2), 47.8 (CH_2—SO_2), 48.9 (SO_2—CH_2), 57.3 (*C*H_2—CO), 58.7 (CH_2—OH), 164.5 (CO-NH), 129.5, 131.1, 134.2, 139.7 (aromatic carbons)
8c	3.19 (t, 2H, NH—C*H*$_2$, J = 4.1 Hz), 3.32 (t, 2H, C*H*$_2$—OH, J = 4.1 Hz), 3.56 (t, 2H, CH_2—SO_2, J = 4.6 Hz), 3.69 (t, 2H, SO_2—CH_2, J = 4.6 Hz), 4.30 (s, 2H, CH_2—CO), 4.68 (bs, 1H, OH), 7.65–7.99 (m, 4H, Ar-H), 8.43 (bs, 1H, NH)	43.1 (NH—CH_2), 47.1 (CH_2—SO_2), 48.0 (SO_2—CH_2), 57.8 (*C*H_2—CO), 59.7 (CH_2—OH), 163.7 (CO-NH), 128.7, 131.3, 133.8, 137.9 (aromatic carbons)
9a	3.28 (t, 2H, NH—C*H*$_2$, J = 4.4 Hz), 3.60 (t, 2H, CH_2—Cl, J = 4.4 Hz), 3.69 (t, 2H, SO_2—CH_2, J = 5.1 Hz), 3.74 (t, 2H, CH_2—SO_2, J = 5.1 Hz), 4.31 (s, 2H, CH_2—CO), 7.64–7.88 (m, 5H, Ar-H), 8.73 (bs, 1H, NH).	42.1 (NH—CH_2), 44.9 (CH_2—SO_2), 45.8 (CH_2—Cl), 47.5 (SO_2—CH_2), 59.7 (*C*H_2—CO), 163.8 (CO—NH), 129.1, 131.4, 134.4, 137.6 (aromatic carbons).
9b	2.41 (s, 3H, Ar-CH_3), 3.35 (t, 2H, NH—C*H*$_2$, J = 4.3 Hz), 3.75 (t, 2H, CH_2—Cl, J = 4.3 Hz), 3.79 (t, 2H, CH_2—SO_2, J = 4.8 Hz), 3.81 (t, 2H, SO_2—CH_2, J = 4.8 Hz), 4.38 (s, 2H, CH_2—CO), 7.70–7.98 (m, 4H, Ar-H), 8.95 (bs, 1H, NH)	24.1 (Ar-CH_3), 41.0 (NH—CH_2), 44.7 (CH_2—SO_2), 46.1 (CH_2—Cl), 48.4 (SO_2—CH_2), 59.1 (*C*H_2—CO), 164.3 (CO—NH), 130.2, 131.7, 134.6, 139.5 (aromatic carbons)
9c	3.32 (t, 2H, NH—C*H*$_2$, J = 4.5 Hz), 3.54 (t, 2H, CH_2—Cl, J = 4.5 Hz), 3.59 (t, 2H, SO_2—CH_2, J = 5.0 Hz), 3.74 (t, 2H, CH_2—SO_2, J = 5.0 Hz), 4.34 (s, 2H, CH_2—CO), 7.60–7.97 (m, 4H, Ar-H), 8.95 (bs, 1H, NH)	40.6 (NH—CH_2), 43.7 (CH_2—SO_2), 44.5 (CH_2—Cl), 46.4 (SO_2—CH_2), 58.1 (*C*H_2—CO), 165.0 (CO—NH), 128.7, 130.6, 134.1, 138.0 (aromatic carbons)
10a	2.82 (t, 2H, C_4—H, J = 4.5 Hz), 3.57 (t, 2H, C_5—H, J = 4.5 Hz), 3.62 (t, 2H, CH_2—SO_2, J = 5.2 Hz), 3.67 (t, 2H, SO_2—CH_2, J = 5.2 Hz), 3.79 (s, 2H, CH_2—C=), 7.66–7.80 (m, 5H, Ar-H)	42.96 (CH_2—SO_2), 47.31 (SO_2—CH_2), 50.1 (C-4), 59.3 (*C*H_2—C=), 62.3 (C-5), 164.6 (C-2), 127.8, 129.6, 134.3, 138.1 (aromatic carbons)
10b	2.32 (s, 3H, Ar-CH_3), 2.85 (t, 2H, C_4—H, J = 4.3 Hz), 3.50 (t, 2H, C_5—H, J = 4.3 Hz), 3.69 (t, 2H, CH_2—SO_2, J = 5.0 Hz), 3.73 (t, 2H, SO_2—CH_2, J = 5.0 Hz), 3.80 (s, 2H, CH_2—C=), 7.56–7.99 (m, 4H, Ar-H)	22.9 (Ar-CH_3), 43.8 (CH_2—SO_2), 47.4 (SO_2—CH_2), 51.5 (C-4), 59.8 (*C*H_2—C=), 63.1 (C-5), 163.8 (C-2), 128.2, 130.0, 133.9, 138.5 (aromatic carbons)
10c	2.79 (t, 2H, C_4—H, J = 4.4 Hz), 3.52 (t, 2H, C_5—H, J = 4.4 Hz), 3.67 (t, 2H, CH_2—SO_2, J = 4.9 Hz), 3.70 (t, 2H, SO_2—CH_2, J = 4.9 Hz), 3.81 (s, 2H, CH_2—C=), 7.60–7.92 (m, 4H, Ar-H)	43.0 (CH_2—SO_2), 46.9 (SO_2—CH_2), 50.8 (C-4), 58.9 (*C*H_2—C=), 63.4 (C-5), 163.5 (C-2), 128.1, 129.3, 133.8, 137.8 (aromatic carbons)

(*Continued*)

Table 3
(Continued)

Compound	^{1}H NMR (δ, ppm)	^{13}C NMR (δ, ppm)
11a	3.25 (t, 2H, S—CH_2, *J* = 4.1 Hz), 3.35 (t, 2H, CH_2—NH_2, *J* = 4.1 Hz), 3.65 (t, 2H, CH_2—SO_2, *J* = 5.8 Hz), 3.78 (t, 2H, SO_2—CH_2, *J* = 5.8 Hz), 4.30 (s, 2H, CH_2—CO), 5.48 (s, 2H, NH_2), 7.59–7.98 (m, 5H, Ar-H)	38.5 (CH_2—NH_2), 41.7 (S—CH_2), 45.8 (SO_2—CH_2), 47.6 (CH_2—SO_2), 59.4 (*C*H_2—CO), 182.3 (CO), 129.5, 131.6, 134.2, 137.4 (aromatic carbons)
11b	2.38 (s, 3H, Ar-CH_3), 3.31 (t, 2H, S—CH_2, *J* = 4.5 Hz), 3.40 (t, 2H, CH_2—NH_2, *J* = 4.5 Hz), 3.60 (t, 2H, CH_2—SO_2, *J* = 6.0 Hz), 3.72 (t, 2H, SO_2—CH_2, *J* = 6.0 Hz), 4.37 (s, 2H, CH_2—CO), 5.39 (s, 2H, NH_2), 7.69–8.05 (m, 4H, Ar-H)	23.9 (Ar-CH_3), 37.9 (CH_2—NH_2), 42.4 (S—CH_2), 46.7 (SO_2—CH_2), 47.9 (CH_2—SO_2), 58.9 (*C*H_2—CO), 181.3 (CO), 128.2, 130.7, 134.8, 139.1 (aromatic carbons)
11c	3.36 (t, 2H, S—CH_2, *J* = 4.3 Hz), 3.38 (t, 2H, CH_2—NH_2, *J* = 4.3 Hz), 3.66 (t, 2H, CH_2—SO_2, *J* = 5.6 Hz), 3.76 (t, 2H, SO_2—CH_2, *J* = 5.6 Hz), 4.41 (s, 2H, CH_2—CO), 5.46 (s, 2H, NH_2), 7.62–8.01 (m, 4H, Ar-H)	37.8 (CH_2—NH_2), 42.4 (S—CH_2), 45.1 (SO_2—CH_2), 48.2 (CH_2—SO_2), 58.4 (*C*H_2—CO), 182.7 (CO), 128.1, 131.0, 134.9, 138.0 (aromatic carbons)
12a	2.91 (t, 2H, C_4—H, *J* = 4.4 Hz), 3.10 (t, 2H, C_5—H, *J* = 4.4 Hz), 3.65 (t, 2H, CH_2—SO_2, *J* = 5.9 Hz), 3.70 (t, 2H, SO_2—CH_2, *J* = 5.9 Hz), 3.81 (s, 2H, CH_2—C=), 7.60–7.91 (m, 5H, Ar-H)	38.1 (C-5), 46.3 (CH_2—SO_2), 47.1 (so_2—CH_2), 52.4 (C-4), 58.7 (*C*H_2—C=), 162.9 (C-2), 129.1, 130.6, 134.8, 137.3 (aromatic carbons)
12b	2.29 (s, 3H, Ar-CH_3), 2.86 (t, 2H, C_4—H, *J* = 4.6 Hz), 3.18 (t, 2H, C_5—H, *J* = 4.6 Hz), 3.59 (t, 2H, CH_2—SO_2, *J* = 5.5 Hz), 3.68 (t, 2H, SO_2—CH_2, *J* = 5.5 Hz), 3.85 (s, 2H, CH_2—C=), 7.67–8.07 (m, 4H, Ar-H)	24.5 (Ar-CH_3), 37.8 (C-5), 46.9 (CH_2—SO_2), 47.6 (so_2—CH_2), 53.0 (C-4), 59.1 (*C*H_2—C=), 163.7 (C-2), 128.1, 131.4, 134.0, 139.7 (aromatic carbons)
12c	2.90 (t, 2H, C_4—H, *J* = 4.2 Hz), 3.15 (t, 2H, C_5—H, *J* = 4.2 Hz), 3.59 (t, 2H, CH_2—SO_2, *J* = 5.7 Hz), 3.76 (t, 2H, SO_2—CH_2, *J* = 5.7 Hz), 3.84 (s, 2H, CH_2—C=), 7.55–8.03 (m, 4H, Ar-H)	38.7 (C-5), 47.0 (CH_2—SO_2), 48.1 (so_2—CH_2), 52.8 (C-4), 58.4 (*C*H_2—C=), 164.5 (C-2), 129.7, 130.9, 133.7, 138.5 (aromatic carbons)

obtain pure *S*-2-aminoethyl 2-(2-(phenylsulfonyl)ethylsulfonyl)-ethanethioate (**11a**; 66%), mp120–122 °C; *S*-2-aminoethyl 2-(2-tosylethylsulfonyl) ethanethioate (**11b**; 69%), mp 116–118 °C; and *S*-2-aminoethyl 2-(2-(4-chlorophenylsulfonyl)ethylsulfonyl)-ethanethioate (**11c**; 65%), mp 126–128 °C.

2-((2-(Arylsulfonyl)ethylsulfonyl)methyl)-4,5-dihydrothiazole (12). *General procedure.* To a solution of *S*-2-aminoethyl 2-(2-(phenylsulfonyl)ethylsulfonyl)-ethanethioate (**11**; 2 mmol) in tetrahydrofuran (6 mL), a catalytic amount of sodium hydride was added and refluxed for 7–10 h. The reaction mixture was concentrated, cooled, and poured onto crushed ice. The solid obtained was filtered, dried, and recrystallized from methanol.

One-pot methodology for synthesis of 2-oxazolines and 2-thiazolines by using Samarium (III) chloride (Method B). ***2-((2-(Arylsulfonyl)ethylsulfonyl)methyl)-4,5-dihydrooxazole (10).*** *General procedure.* To a flask charged with anhydrous samarium (III) chloride (0.1 mmol) and dry toluene (10 mL), 2-aminoethanol (2 mmol) was added followed by *n*-butyllithium (2.2 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min and heated to reflux. Then, methyl 2-(2-(arylsulfonyl)ethylsulfonyl) acetate (**7**; 1 mmol) was added to the contents and continued refluxion for an additional period of 6–9 h. The suspension was cooled to room temperature and filtered. The filtrate was extracted with chloroform, washed with water followed by brine solution. The solvent was removed *in vacuo*. The solid obtained was purified by column chromatography (silica gel, ethyl acetate:hexane, 1:3).

2-((2-(Arylsulfonyl)ethylsulfonyl)methyl)-4,5-dihydrothiazole (12). *General procedure.* To a flask charged with anhydrous samarium (III) chloride (0.1 mmol) and dry toluene (10 mL), 2-aminoethanethiol (2 mmol) was added followed by *n*-butyllithium (2.2 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min and heated to reflux. Then, methyl 2-(2-(arylsulfonyl)ethylsulfonyl)acetate (**7**; 1 mmol) was added to the contents and continued refluxion for an additional period of 6–9 h. The suspension was cooled to room temperature and filtered. The filtrate was extracted with chloroform, washed with water followed by brine solution. The solvent was removed *in vacuo*. The solid obtained was purified by column chromatography (silica gel, ethyl acetate:hexane, 1:3).

One-pot methodology for the synthesis of 2-oxazolines and 2-thiazolines under microwave irradiation (Method C). ***2-((2-(Arylsulfonyl)ethylsulfonyl)methyl)-4,5-dihydrooxazole (10).*** *General procedure.* A mixture of 2-(2-(arylsulfonyl)ethylsulfonyl) acetic acid (**6**; 10 mmol) and 2-aminoethanol (10 mmol) were placed in a Pyrex flask in such a way as to occupy only 10% of the overall volume. The mixture was irradiated using the multimode at 540 watts for 3 min and monitored by TLC. When all the starting material had disappeared, the irradiation was terminated, and the mixture was brought to room temperature. To this, dichloromethane was added and filtered. The resultant compound obtained by evaporation of the solvent under reduced pressure was purified by column chromatography (silica gel, ethyl acetate:hexane, 1:2.5).

2-((2-(Arylsulfonyl)ethylsulfonyl)methyl)-4,5-dihydrothiazole (12). *General procedure.* The compound 2-(2-(arylsulfonyl) ethylsulfonyl)acetic acid (**6**; 10 mmol) and 2-aminoethanethiol (10 mmol) were placed in a Pyrex flask in such a way as to occupy only 10% of the overall volume. The mixture was irradiated at 560 watts for 4 min and monitored by TLC. When all the starting material had disappeared, the irradiation was terminated, and the mixture was allowed to cool to room temperature. The dichloromethane was added to the resulting mixture and filtered. The compound obtained after evaporation of the solvent under vacuum was purified by column chromatography (silica gel, ethyl acetate:hexane, 1:2.5).

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