A Highly Efficient Methodology for 5-Methyl-3-aryl-2-thiooxazolidin-4-ones Using Lithium Perchlorate in DIPEA Mediated Synthesis

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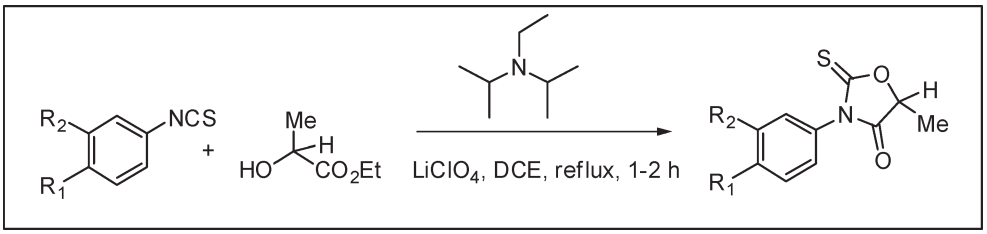

An efficient methodology for the synthesis of 5-methyl-3-aryl-2-thiooxazolidin-4-ones from aryl isothiocyanates has been developed. Aryl isothiocyanates, synthesized from various anilines, were converted to the desired compounds by treating with ethyl lactate in presence of DIPEA and catalytic amount of lithium perchlorate. This method provides a convenient and cost-effective strategy, with no specific purification protocol.

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INTRODUCTION

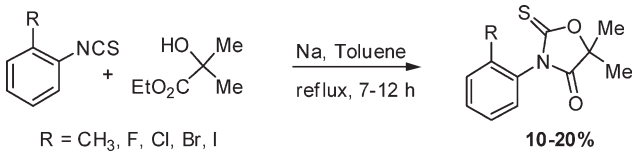
Oxazolidinones and thiooxazolidinones form an integral part of many drugs/intermediates [1,2]. They are well known as chiral directing agents in asymmetric synthesis [3,4]. Thiooxazolidinones were reported for various activities such as potassium channel openers [5], antidiabetics [2], and anticonvulsants [6]. A perusal of the literature shows that there is no report on the synthesis of 3-aryl-2-thiooxazolidin-4-ones having an α-proton, and the available methods in the case of 5,5-dimethyl-3-aryl-2-thiooxazolidin-4-ones, which lack α-protons are poor yielding (Scheme 1) [7–10]. Above all, the reported strategies relied on the kind of isothiocyanates used, and an extrapolation of the methodology to some of the substrates discussed in this article failed primarily due to the harsh reaction conditions [7,8] and the strong base employed [9], leading to the formation of very little of the desired product [10] together with unwanted side-products. The tight legislation on the maintenance of greenness in synthetic pathways and processes demands to prevent waste and minimize energy requirements which unfortunately could not be met in uneconomical low yielding reactions [11].

RESULTS AND DISCUSSION

Various aryl isothiocyanates 2(a–j) were prepared by previously reported method [12] from corresponding anilines 1(a–j). A model reaction of 4-chlorophenyl isothiocyanate with ethyl lactate was experimented under various reaction conditions like sodium hydride, potassium-*tert*-butoxide, sodium metal, potassium hydroxide, 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU), and *N*,*N*-diisopropylethylamine (DIPEA) (Experiments 1–6; Table 1), but the yields obtained were quite disappointing. This prompted us to employ an alternate strategy based on the assumption that the condensation between the reactants would become more facile if their reactivity could be enhanced by adequate co-ordination. Quite interestingly, as in agreement with our notion, a stirring solution of 4-chlorophenyl isothiocyanate and ethyl lactate in dichloroethane (DCE) when refluxed in presence of DIPEA and lithium perchlorate (Scheme 2) showed a drastic improvement in the yields (Experiments 8–10; Table 1); though the product was not formed when either of these was solely employed (Experiments 6 and 7; Table 1).

From the results obtained a plausible reaction mechanism could be depicted as shown in Figure 1. Lithium co-ordinates with the hydroxyl group of ethyl lactate forming the O—Li bond and simultaneously generates perchloric acid which reacts with DIPEA to produce the protonated base and perchlorate anion. Further, the alkoxide attacks the thiocarbonyl carbon of the aryl isothiocyanate resulting in an intramolecular cyclization followed by the protonation of the ethoxy group thereby expelling it as a good leaving group to afford

Scheme 1. Reported strategy for the synthesis of 5,5-dimethyl-3-aryl-2-thiooxazolidin-4-ones lacking α-proton.



5-methyl-3-aryl-2-thiooxazolidin-4-ones with the regeneration of lithium perchlorate in the final step.

Since lithium shows diagonal relationship with magnesium; magnesium perchlorate was also tested, but the reaction afforded poor results and so was the case with zinc perchlorate (Experiments 12 and 13; Table 1). Surprisingly, comparative results could not be obtained when lithium perchlorate was used with triethylamine (TEA) instead of DIPEA (Experiment 11; Table 1). The reason could be attributed to DIPEA having more basic character over TEA. Also the higher boiling point of DIPEA is advantageous under the reflux conditions. The Lewis acid catalyst lithium perchlorate was chosen based on the well known fact that lithium possess better co-ordination power due to its least ionic radius (0.76 Å) than other alkali metals and therefore the higher charge:size ratio increases its covalent character. Also lithium perchlorate is cheap, commercially available and soluble in various organic solvents. The efficiency of lithium perchlorate is well established in various reactions like Diels-Alder reaction [13,14], Friedel-Crafts acylation [15], aminophosphonation of aldehydes [16], Baylis-Hillman reaction [17], aromatic and heteroatom acylation [18], and Nazarov cyclization [19].

Further studies were carried out to determine the stoichiometric quantity of the functional group activator. Based on percentage conversion calculated from GC-MS traces at various concentrations of 0.1, 0.2, 0.6, and 1.2 equivalent of $LiClO_4$ (Fig. 2); it was ascertained that 0.2 equivalent of the Lewis acid would suffice the purpose. We also observed that solvents have a profound influence over the course of the reaction (Table 2). The reaction failed in polar protic medium. Aprotic solvents like toluene and benzene afforded the product in good yields while 1,2-dichloroethane turned out to be the best.

To generalize the methodology the standardized condition was employed on various substituted aryl isothiocyanates, and the respective products were obtained in good yields though the nature of the substituents was found to affect the course of the reaction.

Electron withdrawing functional groups which generally increase the electrophilicity of aryl isothiocyanate provided better yields (Entries 1–7; Table 3), where as electron donating groups led to longer reaction time

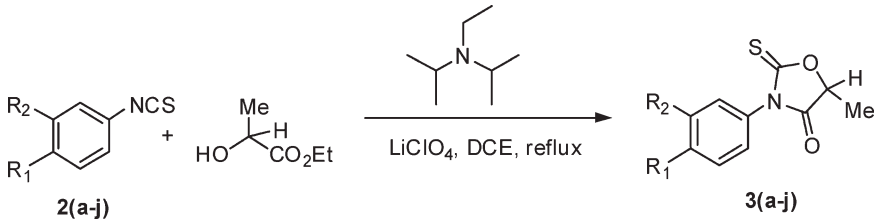
Table 1

Effect of reagent/catalyst in the synthesis of 5-methyl-3-aryl-2-thiooxazolidin-4-one.[a]

	Reaction condition				
Experiment	Reagent[c]	Catalyst[d]	Solvent	% conv. (GC-MS)	Isolated yield (%)[b]
1	NaH	–	DMF	15	10
2	KO*t*Bu	–	DMF	15	12
3	Na[d]	–	Toluene	24	23
4	KOH	–	DMF	15	10
5	DBU	–	DCE	20	10
6	DIPEA	–	DCE	0	0
7	–	$LiClO_4$	DCE	0	0
8	DIPEA	$LiClO_4$[c]	DCE	89	88
9	DIPEA	$LiClO_4$[e]	DCE	88	87
10	DIPEA	$LiClO_4$	DCE	92	90
11	TEA	$LiClO_4$	DCE	71	70
12	DIPEA	$Mg(ClO_4)_2$	DCE	25	20
13	DIPEA	$Zn(ClO_4)_2.\ 6H_2O$	DCE	40	30

[a] The reaction was carried out by stirring a mixture of 4-chlorophenyl isothiocyanate (1.18 mmol, 1.0 equiv) and ethyl lactate (1.42 mmol, 1.2 equiv) in presence of reagent and/or catalyst and solvent (10 mL) at room temperature for 10 min and then refluxing for 1 h.
[b] The product was characterized by NMR and mass spectroscopic methods.
[c] 1.2 equiv was used.
[d] 0.2 equiv was used.
[e] 0.6 equiv was used.

Scheme 2. Synthesis of 5-methyl-3-aryl-2-thiooxazolidin-4-ones.



with lesser yields (Entries 8–10; Table 3). The reaction conditions were also compatible with disubstituted aryl isothiocyanates (Entries 6–7 and 9–10; Table 3).

In conclusion, an efficient and viable synthetic strategy for synthesis of 5-methyl-3-aryl-2-thiooxazolidin-4-ones has been developed.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz, respectively on a Bruker Avance DPX 400 (400 MHz) spectrometer in $CDCl_3$ using TMS as an internal standard. The chemical shifts (δ) for ^{1}H and ^{13}C are given in ppm relative to residual signals of the solvent ($CHCl_3$). Coupling constants are given in Hz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; m, multiplet; bs, broad signal. The IR spectra were recorded on a Nicolet Impact 400 spectrometer as KBr pellets for solid samples. Mass spectra were recorded on POLARIS Q (Thermo Scientific) GC-MSMS spectrometer and elemental analyses were done by Varion-EL elemental analyzer. The reactions were monitored by TLC (Merck). Evaporation of solvents was performed under reduced pressure using a Buchi rotary evaporator. Melting points are uncorrected.

Commercial grade reagents and solvents were used without further purification; ethyl lactate, lithium perchlorate, zinc perchlorate hexahydrate, magnesium perchlorate, 4-fluoro-3-chloroaniline, 4-chloro-3-trifluoromethylaniline (Aldrich), *N,N*-diisopropylethylamine, triethylamine, 4-bromoaniline, 4-fluoroaniline, 4-aminobenzonitrile, 4-methylaniline, 3,4-dimethylaniline, 3,4-dimethoxyaniline, thiophosgene, sodium metal, sodium hydride (60% suspension in mineral oil), potassium *tert*-butoxide, DBU, 1,4-dioxane, (Spectrochem); 4-chloroaniline (Merck); sodium hydrogen carbonate, THF, toluene (CDH); DCE (Loba Chemie), DME (Sigma), benzene, DMF (SISCO), 3-nitroaniline (S.D. Fine chemicals), potassium hydroxide (Qualigens).

General procedure for the synthesis of aryl isothiocyanates. In a 100 mL RB flask, a solution of sodium hydrogen carbonate (5.5 g, 65.7 mmol) in 20 mL water was stirred for 10 min and to it dichloromethane (20 mL) was added followed by 4-chloroaniline (2.0 mL, 21.9 mmol). The reaction mixture was cooled to 0°C, thiophosgene (2.5 mL, 32.85 mmol) was introduced dropwise over a period of 30 min and continuously stirred at room temperature for 1 h. The workup of the reaction mixture was carried out in dichloromethane and dried over anhydrous sodium sulphate. The organic layer upon concentration afforded a crude gummy compound,

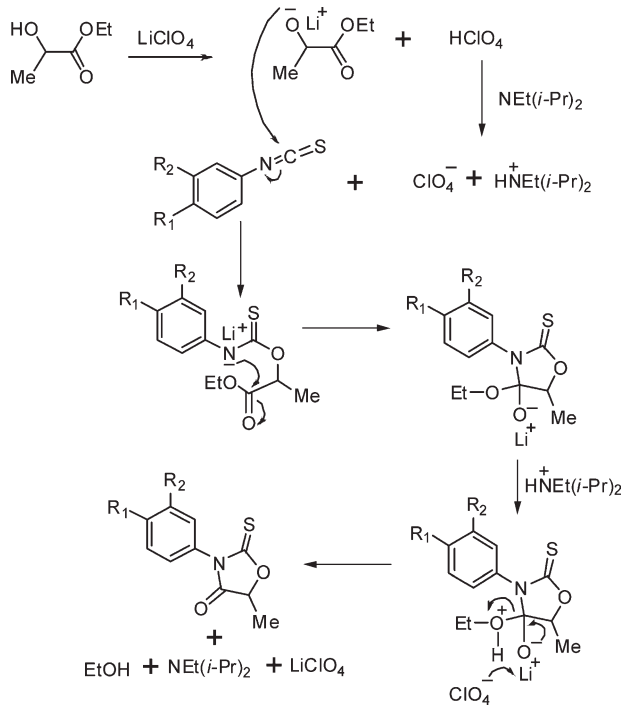


Figure 1. A plausible reaction mechanism for the formation of 5-methyl-3-aryl-2-thiooxazolidin-4-ones.

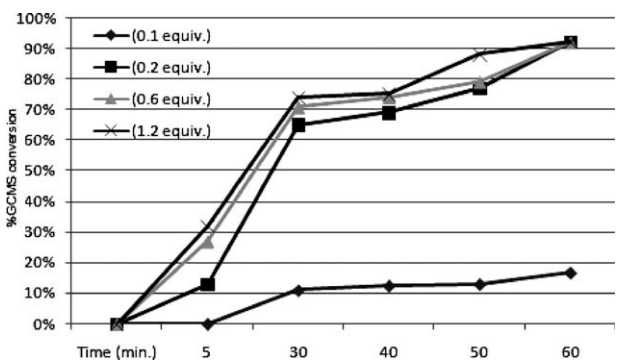


Figure 2. GC-MS study of model reaction at various concentrations of $LiClO_4$.

Table 2

Effect of solvent in the synthesis of 5-methyl-3-aryl-2-thiooxazolidin-4-one.[a]

Experiment	Reagent[b]	Catalyst[c]	Solvent	% conv. (GC-MS)	Isolated yield (%)[d]
1	DIPEA	$LiClO_4$	Neat (80°C)	10	10
2	DIPEA	$LiClO_4$	Toluene	85	81
3	DIPEA	$LiClO_4$	Benzene	86	83
4	DIPEA	$LiClO_4$	DME	70	66
5	DIPEA	$LiClO_4$	DCE	92	90
6	DIPEA	$LiClO_4$	Dioxane	85	81
7	DIPEA	$LiClO_4$	THF	36	33
8	DIPEA	$LiClO_4$	DMF	0	0
9	DIPEA	$LiClO_4$	DMSO	0	0
10	DIPEA	$LiClO_4$	Ethanol	0	0
11	DIPEA	$LiClO_4$	Methanol	0	0

[a] The reaction was carried out by stirring a mixture of 4-chlorophenyl isothiocyanate (1.18 mmol, 1.0 equiv) and ethyl lactate (1.42 mmol, 1.2 equiv) in presence of reagent and/or catalyst and solvent (10 mL) at room temperature for 10 min and then refluxing for 1 h.
[b] 1.2 equiv was used.
[c] 0.2 equiv was used.
[d] The product was characterized by NMR and mass spectroscopic methods.

which was recrystallized in hexane under cold condition. The precipitate was filtered and dried to get the desired compound (Yield: 3.0 g, 81%, white solid). The formation of the product was confirmed by analytical and spectral methods.

4-Chlorophenyl isothiocyanate (2a). Yield: 81%, white solid; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 7.16 (d, J = 8.8 Hz, 2H), 7.33 (d, J = 8.8 Hz, 2H); MS (*m*/*z*): 169.03 (M^+).

4-Bromophenyl isothiocyanate (2b). Yield: 82%, white solid; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 7.10 (d, J = 8.8 Hz, 2H), 7.48 (d, J = 8.8 Hz, 2H); MS (*m*/*z*): 213.03 (M^+), 215.03 (M^{+2}).

4-Fluorophenyl isothiocyanate (2c). Yield: 81%, colourless oil; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 7.00–7.09 (m, 2H), 7.19–7.24 (m, 2H); MS (*m*/*z*): 153.14 (M^+).

4-Cyanophenyl isothiocyanate (2d). Yield: 79%, white solid; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 7.31 (d, J = 8.8 Hz, 2H), 7.66 (d, J = 8.8 Hz, 2H); MS (*m*/*z*): 160.07 (M^+).

3-Nitrophenyl isothiocyanate (2e). Yield: 75%, yellow solid; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.8 Hz, 2H), 8.06 (s, 1H), 8.10–8.15 (m, 1H); MS (*m*/*z*): 180.09 (M^+).

3-Chloro-4-fluorophenyl isothiocyanate (2f). Yield: 75%, colourless oil; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 7.09–7.16 (m, 2H), 7.29–7.37 (m, 1H); MS (*m*/*z*): 187.01 (M^+).

4-Chloro-3-trifluoromethylphenyl isothiocyanate (2g). Yield: 70%, colourless oil; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 7.31–7.34 (m, 1H), 7.42–7.54 (m, 2H); MS (*m*/*z*): 237.07 (M^+).

4-Methylphenyl isothiocyanate (2h). Yield: 90%, brownish solid; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 2.36 (s, 3H), 7.11–7.16 (m, 4H); MS (*m*/*z*): 149.08 (M^+).

3,4-Dimethylphenyl isothiocyanate (2i). Yield: 92%, brown oil; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 2.26 (s, 6H), 6.97 (d, J = 8.0 Hz, 1H), 7.02 (s, 1H), 7.09 (d, J = 8.0 Hz, 1H); MS (*m*/*z*): 163.09 (M^+).

Table 3

Synthesis of 5-methyl-3-aryl-2-thiooxazolidin-4-ones.[a]

Entry	Aryl isothiocyanate	R_1	R_2	Reaction time (h)	Product	% conv. (GC-MS)	Isolated yield (%)[b]
1	2a	Cl	H	1.0	3a	92	90
2	2b	Br	H	1.5	3b	77	75
3	2c	F	H	1.0	3c	87	85
4	2d	CN	H	1.5	3d	82	80
5	2e	H	NO_2	1.5	3e	79	75
6	2f	F	Cl	2.0	3f	70	69
7	2g	Cl	CF_3	2.0	3g	74	72
8	2h	Me	H	1.0	3h	70	65
9	2i	Me	Me	1.5	3i	78	70
10	2j	MeO	MeO	1.5	3j	71	70

[a] The reaction was carried out by stirring a mixture of aryl isothiocyanate (1.18 mmol, 1.0 equiv) and ethyl lactate (1.42 mmol, 1.2 equiv) in presence of DIPEA (1.42 mmol, 1.2 equiv) and $LiClO_4$ (0.24 mmol, 0.2 equiv) in DCE (10 mL) at room temperature for 10 min and then refluxing for 1–2 h.
[b] The product was characterized by NMR and mass spectroscopic methods.

3,4-Dimethoxyphenyl isothiocyanate (2j). Yield: 88%, white solid; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 3.37 (s, 6H), 6.65 (s, 1H), 6.69–6.75 (m, 2H); MS (*m*/*z*): 195.14 (M^+).

General procedure for the synthesis of 5-methyl-3-aryl-2-thiooxazolidin-4-one. To a solution of 4-chlorophenyl isothiocyanate (0.2 g, 1.18 mmol, 1.0 equiv) in 1,2-dichloroethane (10 mL), ethyl lactate (0.17 mL, 1.42 mmol, 1.2 equiv), *N*,*N*-diisopropylethylamine (0.24 mL, 1.42 mmol, 1.2 equiv), and lithium perchlorate (0.026 g, 0.24 mmol, 0.2 equiv) were added. It was refluxed for 1 h, and the reaction mixture was cooled, washed with water, and concentrated. The crude product was dissolved in minimum amount of dichloromethane, precipitated with excess of hexane, filtered, and dried (Yield: 0.26 g, 90%, white solid). The compound was identified by spectral and analytical methods.

5-Methyl-3-(4-chlorophenyl)-2-thiooxazolidin-4-one (3a). Yield: 90%, white solid; mp 111–114°C; FTIR (KBr) ν: 1763 cm^{-1}; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 1.77 (d, J = 6.8 Hz, 3H), 5.11–5.17 (m, 1H), 7.30 (d, J = 8.8 Hz, 2H), 7.51 (d, J = 8.8 Hz, 2H); NMR (^{13}C, 100 MHz, $CDCl_3$) δ 16.66, 78.71, 128.86, 129.78, 130.64, 135.84, 172.91, 188.79; MS (*m*/*z*): 241.00 (M^+); $C_{10}H_8ClNO_2S$ Calcd: C, 49.69; H, 3.34; N, 5.80; S, 13.27; Found: C, 49.72; H, 3.38; N, 5.85; S, 13.33.

5-Methyl-3-(4-bromophenyl)-2-thiooxazolidin-4-one (3b). Yield: 75%, white solid; mp 144–147°C; FTIR (KBr) ν: 1771 cm^{-1}; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 1.78 (d, J = 7.2 Hz, 3H), 5.12–5.17 (m, 1H), 7.24 (d, J = 8.8 Hz, 2H), 7.67 (d, J = 8.8 Hz. 2H); NMR (^{13}C, 100 MHz, $CDCl_3$) δ 16.67, 78.74, 123.96, 129.12, 131.16, 132.77, 172.86, 188.71; MS (*m*/*z*): 285.01(M^+), 287.01(M^{+2}); $C_{10}H_8BrNO_2S$ Calcd: C, 41.97; H, 2.82; N, 4.89; S, 11.21; Found: C, 41.95; H, 2.80; N, 4.94; S, 11.23.

5-Methyl-3-(4-fluorophenyl)-2-thiooxazolidin-4-one (3c). Yield: 85%, white solid; mp 93–96°C; FTIR (KBr) ν: 1771 cm^{-1}; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 1.76 (d, J = 6.8 Hz, 3H), 5.11–5.16 (m, 1H), 7.19–7.25 (m, 2H), 7.30–7.35 (m, 2H); NMR (^{13}C, 100 MHz, $CDCl_3$) δ 16.63, 78.69, 116.51, 116.74, 129.49, 129.58, 161.66, 164.15, 173.08, 189.16; MS *m*/*z*: 225.10 (M^+); $C_{10}H_8FNO_2S$ Calcd: C, 53.32; H, 3.58; N, 6.22; S, 14.24; Found: C, 53.35; H, 3.55; N, 6.27; S, 14.26.

5-Methyl-3-(4-cyanophenyl)-2-thiooxazolidin-4-one (3d). Yield: 80%, white solid; mp 202–205°C; FTIR (KBr) ν: 1774, 2231 cm^{-1}; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 1.73 (d, J = 6.8 Hz, 3H), 5.14–5.20 (m, 1H), 7.53 (d, J = 8.8 Hz, 2H), 7.83 (d, J = 8.8 Hz, 2H); NMR (^{13}C, 100 MHz, $CDCl_3$) δ 16.65, 78.83, 113.69, 117.64, 128.49, 133.32, 135.98, 172.46, 187.77; MS (*m*/*z*): 232.10 (M^+); $C_{11}H_8N_2O_2S$ Calcd: C, 56.88; H, 3.47; N, 12.06; S, 13.81; Found: C, 56.92; H, 3.51; N, 12.10; S, 13.86.

5-Methyl-3-(3-nitrophenyl)-2-thiooxazolidin-4-one (3e). Yield: 75%, light yellow solid; mp 151–154°C; FTIR (KBr) ν: 1769 cm^{-1}; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 1.80 (d, J = 7.2 Hz, 3H), 5.19–5.24 (m, 1H), 7.75 (d, J = 8.0 Hz, 2H), 8.30 (s, 1H), 8.34–8.37 (m, 1H); NMR (^{13}C, 100 MHz, $CDCl_3$) δ 16.67, 78.96, 123.22, 124.51, 130.32, 133.19, 133.70, 148.61, 172.52, 187.93; MS (*m*/*z*): 252.08 (M^{+1}); $C_{10}H_8N_2O_4S$ Calcd: C, 47.61; H, 3.20; N, 11.11; S, 12.71; Found: C, 47.67; H, 3.16; N, 11.09; S, 12.68.

5-Methyl-3-(3-chloro-4-fluorophenyl)-2-thiooxazolidin-4-one (3f). Yield: 69%, white solid; mp 98–100°C; FTIR (KBr) ν: 1770 cm^{-1}; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 1.77 (d, J = 7.2 Hz, 3H), 5.12–5.17 (m, 1H), 7.24–7.33 (m, 2H), 7.43–7.46 (m, 1H); NMR (^{13}C, 100 MHz, $CDCl_3$) δ 16.62, 78.78, 117.27, 117.50, 127.71, 127.79, 130.18, 157.28, 159.80, 172.74, 188.51; MS (*m*/*z*): 259.05 (M^+); $C_{10}H_7ClFN_2O_2S$ Calcd: C, 46.25; H, 2.72; N, 5.39; S, 12.35; Found: C, 46.27; H, 2.75; N, 5.43; S, 12.39.

5-Methyl-3-(4-chloro-3-trifluoromethylphenyl)-2-thiooxazolidin-4-one (3g). Yield: 72%, white solid; mp 178–181°C; FTIR (KBr) ν: 1781 cm^{-1}; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 1.80 (d, J = 7.2 Hz, 3H), 5.15–5.20 (m, 1H), 7.52 (d, J = 8.8 Hz, 1H), 7.69 (d, J = 8.8 Hz, 1H), 7.72 (s, 1H); NMR (^{13}C, 100 MHz, $CDCl_3$) δ 16.65, 78.87, 123.42, 127.00, 127.06, 129.92, 130.81, 131.93, 132.61, 172.53, 187.98; MS (*m*/*z*): 309.01 (M^+); $C_{11}H_7ClF_3NO_2S$ Calcd: C, 42.66; H, 2.28; N, 4.52; S, 10.35; Found: C, 42.70; H, 2.31; N, 4.55; S, 10.34.

5-Methyl-3-(4-methylphenyl)-2-thiooxazolidin-4-one (3h). Yield: 65%, white solid; mp 109–111°C; FTIR (KBr) ν: 1769 cm^{-1}; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 1.76 (d, J = 7.2 Hz, 3H), 2.43 (s, 3H), 5.11–5.16 (m, 1H), 7.21 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H); NMR (^{13}C, 100 MHz, $CDCl_3$) δ 16.69, 21.34, 78.67, 127.23, 129.60, 130.22, 140.09, 173.35, 189.63; MS (*m*/*z*): 222.09 (M^{+1}); $C_{11}H_{11}NO_2S$ Calcd: C, 59.71; H, 5.01; N, 6.33; S, 14.49; Found: C, 59.68; H, 5.04; N, 6.28; S, 14.51.

5-Methyl-3-(3,4-dimethylphenyl)-2-thiooxazolidin-4-one (3i). Yield: 70%, white solid; mp 113–115°C; FTIR (KBr) ν: 1769 cm^{-1}; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 1.73 (d, J = 7.2 Hz, 3H), 2.30 (s, 6H), 5.07–5.12 (m, 1H), 7.02 (s, 1H), 7.04 (d, J = 7.6 Hz, 1H), 7.25 (d, J = 7.6 Hz, 1H); NMR (^{13}C, 100 MHz, $CDCl_3$) δ 16.69, 19.69, 19.89, 78.70, 124.76, 128.24, 129.79, 130.69, 138.28, 138.85, 173.46, 189.81; MS (*m*/*z*): 235.09 (M^+); $C_{12}H_{13}NO_2S$ Calcd: C, 61.25; H, 5.57; N, 5.95; S, 13.63; Found: C, 61.21; H, 5.61; N, 5.99; S, 13.65.

5-Methyl-3-(3,4-dimethoxyphenyl)-2-thiooxazolidin-4-one (3j). Yield: 70%, white solid, mp 145–147°C; FTIR (KBr) ν: 1768 cm^{-1}; NMR (^{1}H, 400 MHz, $CDCl_3$) δ 1.76 (d, J = 6.8 Hz, 3H), 3.89 (s, 3H), 3.92 (s, 3H), 5.09–5.14 (m, 1H), 6.80 (s, 1H), 6.87 (d, J = 8.8 Hz, 1H), 6.97 (d, J = 8.8 Hz, 1H); NMR (^{13}C, 100 MHz, $CDCl_3$) δ 16.64, 56.05, 56.13, 78.62, 110.73, 111.20, 120.04, 124.80, 149.55, 150.02, 173.39, 189.76; MS (*m*/*z*): 267.08 (M^+); $C_{12}H_{13}NO_4S$ Calcd: C, 53.92; H, 4.90; N, 5.24; S, 12.00; Found: C, 53.94; H, 4.89; N, 5.30; S, 11.95.

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REFERENCES AND NOTES

[1] Walker, R. B.; Fitz, L. D.; Williams, L. M.; Linton, H.; Smith, C. C. Gen Pharmacol Vasc Syst 1993, 24, 669.

[2] Momose, Y.; Maekawa, T.; Yamano, T.; Kawada, M.; Odaka, H.; Ikeda, H.; Sohda, T. J Med Chem 2002, 45, 1518.

[3] Lin, G. Q.; Li, Y. M.; Chan, A. S. C. Principles and Applications of Asymmetric Synthesis; Wiley Interscience: New York, 2001; p 135.

[4] Aitken, R. A.; Kilenyi, S. N. Asymmetric Synthesis; Blackie Academic & Professional: London, 1992; p 83.

[5] Liang, P.-H.; Hsin, L.-W.; Cheng, C.-Y. Bioorg Med Chem 2002, 10, 3267.

[6] Shapiro, S. L.; Rose, I. M.; Testa, F. C.; Roskin, E.; Freedman, L. J Am Chem Soc 1959, 81, 6498.

[7] Ordu, O. D.; Dogan, I. Tetrahedron: Asymmetry 2004, 15, 925.

[8] Yilmaz, E. M.; Doğan, I. Tetrahedron: Asymmetry 2008, 19, 2184.

[9] Doğan, I.; Burgemeister, T.; Içli, S.; Mannschreck, A. Tetrahedron 1992, 48, 7157.

[10] Ordu, O. D.; Yilmaz, E. M.; Doğan, I. Tetrahedron: Asymmetry 2005, 16, 3752.

[11] Tundo, P.; Anastas, P.; Black, D. S.; Breen, J.; Collins, T.; Memoli, S.; Miyamoto, J.; Polyakoff, M.; Tumas, W. Pure Appl Chem 2000, 72, 1207.

[12] Nair, V. A.; Mustafa, S. M.; Mohler, M. L.; Dalton, J. T.; Miller, D. D. Tetrahedron Lett 2006, 47, 3953.

[13] Reetz, M. T.; Gansäuer, A. Tetrahedron 1993, 49, 6025.

[14] Burke, L. T.; Dixon, D. J.; Ley, S. V.; Rodríguez, F. Org Lett 2000, 2, 3611.

[15] Hachiya, I.; Moriwaki, M.; Kobayashi, S. Tetrahedron Lett 1995, 36, 409.

[16] Heydari, A.; Karimian, A.; Ipaktschi, J. Tetrahedron Lett 1998, 39, 6729.

[17] Kawamura, M.; Kobayashi, S. Tetrahedron Lett 1999, 40, 1539.

[18] Chapman, C. J.; Frost, C. G.; Hartleya, J. P.; Whittleb, A. J. Tetrahedron Lett 2001, 42, 773.

[19] Malona, J. A.; Colbourne, J. M.; Frontier, A. J. Org Lett 2006, 8, 5661.