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Synthesis of New Oxazolidinethiones and Their Ring Opening Reactions

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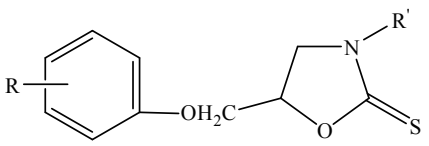
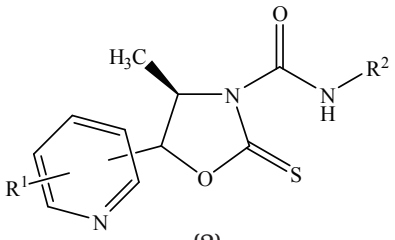
Introduction

Oxazolidinethiones have been the subject of extensive studies because of their important biological activity.[1] The chemistry of oxazolidine-2-thiones has received considerable attention due to the wide variety of biological activities exhibited by their derivatives, namely D-fructose transporter inhibitors[2], antithyroid[3,4], antifertility[5,6], inhibition of dopamine β–hydroxylase (**1**)[7], antibacterial[8,9], insecticidal[10] and herbicidal activities (**2**)[11].



(1)



(2)

In addition, oxazolidinones are a new class of totally synthetic antibacterial compounds. These compounds have been known to inhibit

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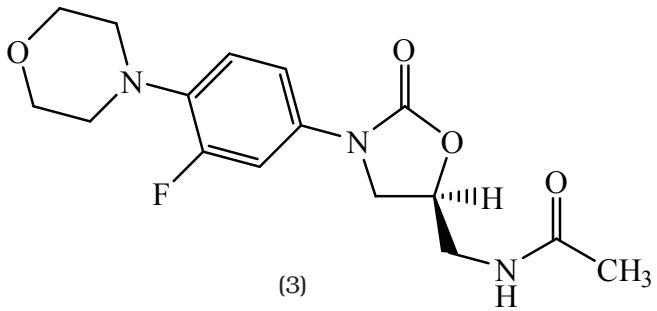
translation at the initiation phase of protein synthesis[12]. Linezolid (**3**) is a member of oxazolidinones and is totally synthetic compound. Oxazolidinthiones are the sulfur analoges of oxazolidinones and the syntheses of their new derivatives are very important in drug chemistry.



(3)

The increasing availability of enantiopure *vic*-aminoalcohols has stimulated interest in developing chemistry which makes use of oxazolidinone / oxazolidinthiones.[13,14] Oxazolidinethiones have been used synthetically in other ways, primarily as chiral auxiliaries,[15,16,17] but also as intermediates in the synthesis of enantiopure protected aryl-β-hydroxyl-α-amino acids[18] and 1-(*Boc*)-amino-1-alkenylphosphonate esters,[19] as a derivative for kinetic resolutions,[20] as pseudo-C-nucleosides,[21] in radical reactions,[22] and as precursors for other oxazolidines.[23] Carbon disulfide,[24] thiophosgene[21,25] or bis(imidazolyl)thione[22,23] have been used to prepare them from the corresponding amino alcohols, as well as hydroxide addition to isothiocyanates[21] and cycloaddition of aldehydes to anions of substituted methyl isothiocyanates.[18,19]

Cyclic thionocarbonates and cyclic sulphate esters are five membered similar heterocycles with oxazolidinethiones. The nucleophilic ring-opening reactions of vicinal diol cyclic thionocarbonates[25] and cyclic sulphate esters[26] with a variety of nucleophiles have been investigated in the literature.

Materials and Methods

β-Amino alcohols **4(a-e)** were converted to their corresponding oxazolidinethiones **5(a-e)** by treatment with thiophosgene and triethylamine

in dichloromethane (DCM) at 0°C. Their ^{13}C nmr spectra showed a C=S resonance at δ: 189.0, and also 5-C resonance at δ: 73.5 - 76.9 and 4-C resonance at δ: 52.5 – 62.4 for the other two ring carbons. N-*t-boc* derivatives **6(a-e)** were obtained via the reactions of oxazolidinethiones **5(a-e)** with triethylamine, di-*tert*-butyl dicarbonate and 4-(dimethylamino)pyridine (DMAP) in dichloromethane. Here, the electron withdrawing N-*t-boc* protection was done to investigate the ring opening capacity of this heterocyclic ring system with nucleophiles.

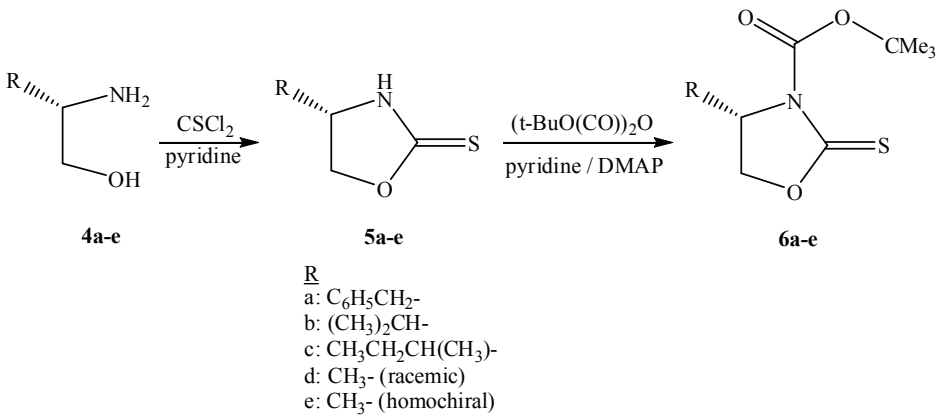


Figure 1
The synthesis of oxazolidine-2-thiones and their *N- t*-boc derivatives.

Some preliminary investigations have been made with nucleophiles on the reactions of cyclic thionocarbamate **6d** and some successful ring opening reactions were observed by breaking of C-O bond of the heterocycle. In general, sulfur is very nucleophilic because of its large size, which makes it readily polarizable, and its lone pairs of electrons are readily accessible. Therefore, thiolate anions are used here as sulfur nucleophiles. The reaction of **6d** and **6e** with phenylthiolate gave the N-*boc* protected esters **7d** and **7e** in yields of 37% and 69% respectively. Besides, the reaction of **6d** with ethylthiolate gave the N-*boc* protected ester **7f** in 25% yield and also gave **7g** and **5e** [(MS (EI) m/z 117 (M^+, 100%), 102, 41)] as side products. **7g** was detected by MS ((EI) m/z 279 (M^+)) which loses carbonyl sulphide (COS) to give **7f**. The ring-opening reactions of other oxazolidinethione derivatives with nucleophiles are still under investigation and they will be reported later.

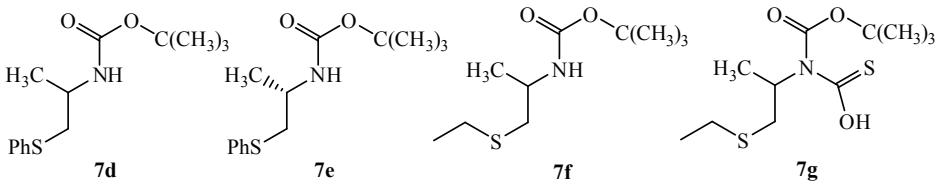


Figure 2
Ring opening products at 5-C position of **6d-e**.

Experimental

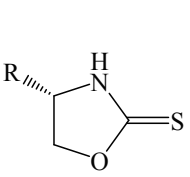
All reagents were of commercial quality and reagent quality solvents were used without further purification. Optical rotations were measured on a Rudolph Research Analytical Autopol IV automatic polarimeter; $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. IR spectra (KBr) were recorded on a Shimadzu FT-IR DR-8001 FT infrared spectrophotometer. NMR spectra were recorded on a Bruker DPX-400 MHz FT-NMR for ^1H and 100 MHz for ^{13}C, with the chemical shifts (δ) reported in parts per million (ppm) relative to TMS and the coupling constants (J) quoted in Hz. $CDCl_3$ was used as a solvent and an internal standard. Mass spectra were obtained on an Agilent 5973 Network Mass Selective Detector via HPP7-M Direct Insertion Probe. The purity of the compounds was assessed by thin-layer chromatography (TLC) on silica gel 60 F_{254}. Column chromatography was conducted on silica gel 60 (mesh size 0.063-0.200 mm). Melting points were measured on a Thomas Hoover Capillary Melting Point Apparatus.

General Synthetic Method for Oxazolidine-2-thiones[27]

Thiophosgene (1.0 mmol) in dichloromethane (2 mL) was added to the stirring solution of β-amino alcohol (**4**) (1.0 mmol) and triethylamine (2.5 mmol) in CH_2Cl_2 (100 mL) at 0°C. After the mixture was stirred for 30 min at 0°C, the reaction was quenched with 10% $NaHSO_4$. The organic phase was separated, washed with 1 M NH_4OH, dried over Na_2SO_4, filtered and concentrated in vacuo. Crude material was purified with column chromatography to afford oxazolidin-2-thion (**5**).

TABLE 1

[1]H-NMR data of **5, 6** and **7** derivatives.



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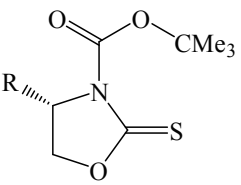

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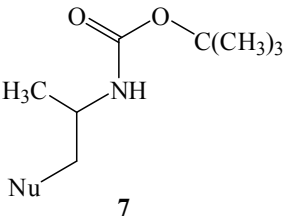

7

[1]H-NMR ($CDCl_3$); δ (ppm); J (Hz)
5a 8.28 (1H, br-s, NH), 7.19 (2H, d, J=7.2 Hz, C_6H_5), 7.31 (3H, 2xt, J=7.3 Hz, C_6H_5), 4.65 (1H, t, J=8.5 Hz, 5-H_α), 4.34 (2H, m, 5-H_β & 4-H), 2.93 (2H, m, CH_2Ph).
5b 9.04 (1H, br-s, NH), 4.71 (1H, t, J=9.1 Hz, 5-H_α), 4.40 (1H, dd, J=6.7 & 9.1 Hz, 5-H_β), 3.93 (1H, m, 4-H), 1.85 (1H, m, CH), 1.00 (3H, d, J=6.8 Hz, CH_3), 0.95 (3H, d, J=6.8 Hz, CH_3).
5c 8.99 (1H, br-s, NH), 4.73 (1H, t, J=8.4 Hz, 5-H_α), 4.18 (2H, m, 5-H_β & 4-H), 1.64 (1H, m, CH), 1.38 (2H, m, CH_2), 0.88 (3H, d, J=4.2 Hz, CH_3), 0.86 (3H, d, J=4.2 Hz, CH_3).
5d 8.63 (1H, br-s, NH), 4.79 (2H, m, 5-H_2), 4.25 (1H, m, 4-H), 1.37 (3H, d, J=5.9 Hz, CH_3).
6a 7.19 (2H, d, J=7.2 Hz, C_6H_5), 7.31 (3H, 2xt, J=7.3 Hz, C_6H_5), 4.69 (1H, m, 4-H), 4.28 (2H, m, 5-H_2), 3.29 (1H, dd, J=3.5 & 13.3 Hz, $CH_\alpha Ph$), 2.83 (1H, dd, J=10.0 & 13.3 Hz, $CH_\beta Ph$), 1.61 (9H, s, $C(CH_3)_3$).
6b 4.33 (3H, m, 4-H & 5-H_2), 2.23 (1H, m, CH), 1.50 (9H, s, 3xCH_3), 0.88 (3H, d, J=7.3 Hz, CH_3), 0.86 (3H, d, J=7.0 Hz, CH_3).
6c 4.37 (2H, m, 5-H_2), 4.09 (1H, m, 4-H), 1.46 (1H, m, CH), 1.40 (9H, s, 3xCH_3), 1.29 (2H, m, CH_2), 0.8 (6H, m, 2xCH_3).
6d 4.60 (1H, m, 4-H), 4.53 (1H, t, J=8.5 Hz, 5-H_α), 4.15 (1H, dd, J=3.0 & 8.5 Hz, 5-H_β), 1.58 (9H, s, $C(CH_3)_3$), 1.46 (3H, d, J=6.2 Hz, CH_3).
6e 4.54 (1H, m, 4-H), 3.51 (1H, dd, J=7.4 & 11.0, 5-H_α), 2.73 (1H, d, J=11.0 Hz, 5-H_β), 1.46 (9H, s, $C(CH_3)_3$), 1.40 (3H, d, J=6.3 Hz, CH_3).
7d 7.26 (5H, m, Ar-H_5), 4.62 (1H, br-s, NH), 3.81 (1H, m, 1-H), 3.05 (1H, dd, J=5.1 & 13.3Hz, 2-H_α), 2.83 (1H, dd, J=6.0 & 13.3Hz, 2-H_β), 1.34 (9H, s, $C(CH_3)_3$), 1.13 (1H, d, J=6.6 Hz, CH_3).
7f 8.96 (1H, br-s, NH), 4.78 (1H, m, 1-H), 4.24 (2H, m, CH_2S), 3.55 (2H, dd, J=5.7 & 10.8Hz, 2-H_2), 1.44 (9H, s, $C(CH_3)_3$), 1.37 (1H, d, J=6.0 Hz, CH_3), 1.15 (3H, d, J=6.7Hz, CH_3CH_2S).

General Synthetic Method for *N- t-boc* Derivatives[28]

Triethylamine (1.0 mmol), di-*tert*-butyl dicarbonate (2.0 mmol) and 4-(dimethylamino)pyridine (1.0 mmol) was added to the stirring solution of oxazolidine-2-thione (**5**) (1.0 mmol) in methylene chloride. The solution was stirred under argon atmosphere at 25°C for 7 hours. Volatilities were removed and the residue was purified on silica gel via routine column chromatography. Elution with ethyl acetate / hexane (1:3) gave N-*tert*-butoxycarbonyl-oxazolidine-2-thiones (**6**).

General Synthetic Method for N-*boc* Protected Esters

Dry thiophenol (1.5 mmol) was added to the stirring solution of sodium methoxide (1.0 mmol) in dry methanol under nitrogen gas. After stirring the mixture for 30 min, the heterocyclic compound **6** (1.0 mmol) was added. After overnight stirring the solvent was removed by rotavapor. Distilled water (20 mL) was added to the residue and the solution was neutralized with dropwise addition of 1M HCl. Neutral solution was extracted with dichloromethane, dried over $MgSO_4$, filtered and concentrated. Crude product was purified with column chromatography.

Results

(4*S*)-4-benzyl-1,3-oxazolidine-2-thione (5a): 4a (0.5 g, 3.38 mmol) was used according to the general method to afford the product as yellow oil (1.1 g, 62%); R_f 0.65 (1:1 EtOAc-hexane), $[\alpha]_{589}^{23}$ = +52.94° (c 0.136, CH_3CN); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ_H 8.28 (1H, br-s, NH), 7.19 (2H, d, J=7.2 Hz, C_6H_5), 7.31 (3H, 2xt, J=7.3 Hz, C_6H_5), 4.65 (1H, t, J=8.5 Hz, 5-H_α), 4.34 (2H, m, 5-H_β & 4-H), 2.93 (2H, m, CH_2Ph); ^{13}C-NMR ($CDCl_3$, 400 MHz) δ_C 189.5 (C=S), 135.3, 129.1, 129.1, 127.4, 74.7 (5-C), 57.8 (4-C), 40.4 (CH_2Ph); IR (KBr) ν_{max} (neat / cm^{-1}) 3028, 1812, 1642, 1515, 1328; MS (EI) m/z 193 (M^+, 83%), 117 ($M+H^+$ - Ph, 11%), 102 (boc+H^+, 98%), 91 ($PhCH_2$, 100%).

(4*S*)-4-isopropyl-1,3-oxazolidine-2-thione (5b): 4b (1.9 g, 18.0 mmol) was used according to the general method to afford the product as yellow oil (2.2 g, 77%); R_f 0.56 (1:2 EtOAc-hexane); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ_H 9.04 (1H, br-s, NH), 4.71 (1H, t, J=9.1 Hz, 5-H_α), 4.40 (1H, dd,

J=6.7 & 9.1 Hz, 5-H_β), 3.93 (1H, m, 4-H), 1.85 (1H, m, CH), 1.00 (3H, d, J=6.8 Hz, CH_3), 0.95 (3H, d, J=6.8 Hz, CH_3); ^{13}C-NMR ($CDCl_3$, 400 MHz) δ_C 189.4 (C=S), 73.5 (5-C), 62.4 (4-C), 31.8 (CH), 17.9 (2xCH_3); IR (KBr) ν_{max} (neat / cm^{-1}) 2963, 1743, 1526, 1272, 1171; MS (EI) m/z 145 (M^+, 100%), 102 (M^+ - $CH(CH_3)_2$, 54%), 42 ($CH(CH_3)_2$ – H, 50%).

(4*S*)-4-*sec*-Butyl-1,3-oxazolidine-2-thione (5c): 4c (1.00 g, 8.53 mmol) was used according to the general method to afford the product as white solid (0.96 g, 71%); mp: 145-153°C, R_f 0.57 (1:2 EtOAc-hexane); $[\alpha]_{589}^{30}$ = -44.18° (c 0.91, MeOH); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ_H 8.99 (1H, br-s, NH), 4.73 (1H, t, J=8.4 Hz, 5-H_α), 4.18 (2H, m, 5-H_β & 4-H), 1.64 (1H, m, CH), 1.38 (2H, m, CH_2), 0.88 (3H, d, J=4.2 Hz, CH_3), 0.86 (3H, d, J=4.2 Hz, CH_3); ^{13}C-NMR ($CDCl_3$, 400 MHz) 189.0 (C=S), 75.8 (5-C), 55.1 (4-C), 43.5 (CH), 25.1 (CH_2), 22.8 (CH_3), 21.8 (CH_3); IR (KBr) ν_{max} (neat / cm^{-1}) 3500, 1792, 1560; MS (EI) m/z 159.0 (M^+, 100%), 117, 102, 57.

4-Methyl-1,3-oxazolidine-2-thione (5d): 4d (0.75 g, 10.0 mmol) was used according to the general method to afford the product as yellow solid (0.32 g, 27%); mp: 77°C, R_f 0.34 (1:2 EtOAc-hexane); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ_H 8.63 (1H, br-s, NH), 4.79 (2H, m, 5-H_2), 4.25 (1H, m, 4-H), 1.37 (3H, d, J=5.9 Hz, CH_3); ^{13}C-NMR ($CDCl_3$, 400 MHz) δ_C 189.3 (C=S), 76.9 (5-C), 52.5 (4-C), 20.0 (CH_3); IR (KBr) ν_{max} (neat / cm^{-1}) 3167, 1532, 1285, 1181; MS (EI) m/z 117 (M^+, 100%), 102, 86, 42.

(4*S*)-4-Methyl-1,3-oxazolidine-2-thione (5e): 4e (1.93 g, 25.6 mmol) was used according to the general method to afford the product as yellow solid (1.09 g, 36%); mp: 77°C, R_f 0.34 (1:2 EtOAc-hexane); $[\alpha]_{589}^{23}$ = +35.28° (c 0.36, MeOH); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ_H 8.63 (1H, br-s, NH), 4.79 (2H, m, 5-H_2), 4.25 (1H, m, 4-H), 1.37 (3H, d, J=5.9 Hz, CH_3); ^{13}C-NMR ($CDCl_3$, 400 MHz) δ_C 189.3 (C=S), 76.9 (5-C), 52.5 (4-C), 20.0 (CH_3); IR (KBr) ν_{max} (neat / cm^{-1}) 3167, 1532, 1285, 1181; MS (EI) m/z 117 (M^+, 100%), 102, 86, 42.

(4*S*)-4-Benzyl-2-thioxo-oxazolidine-3-carboxylic acid *tert*-butyl ester (6a): 5a (0.50 g, 2.59 mmol) was used according to the general method to afford the product as white solid (0.76 g, 100%) and recrystallized from hexane-DCM (1:1); R_f 0.69 (1:2 EtOAc-hexane); $[\alpha]_{589}^{23}$ = +25.34° (c 0.146, MeOH); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ_H 7.19 (2H, d, J=7.2 Hz, C_6H_5), 7.31 (3H, 2xt, J=7.3 Hz, C_6H_5), 4.69 (1H, m, 4-H), 4.28 (2H, m, 5-H_2), 3.29 (1H, dd, J=3.5 & 13.3 Hz, CH_αPh), 2.83 (1H, dd, J=10.0

& 13.3 Hz, $CH_\beta Ph$), 1.61 (9H, s, $C(CH_3)_3$). ^{13}C-NMR ($CDCl_3$, 400 MHz) δ_C 184.3 (C=O), 149.2 (C=S), 135.1, 129.5, 129.3, 129.1, 128.6, 127.4 (Ph), 84.9 (CMe_3), 70.2 (5-C), 60.2 (4-C), 38.4 (CH_2Ph), 28.0 ($3xCH_3$); IR (KBr) ν_{max} (neat / cm^{-1}) 2980, 1759, 1722, 1370; MS (EI) *m/z* 193 ($M+H^+$ - boc, 75%), 117 ($M+H^+$ - Ph, 8%), 102 (boc+H^+, 96%), 91 ($PhCH_2$, 100%).

(4*S*)-4-Isopropyl-2-thioxo-oxazolidine-3-carboxylic acid *tert*-butyl ester (6b): 5b (0.50 g, 3.44 mmol) was used according to the general method to afford the product as yellow solid (0.457 g, 54%); R_f 0.67 (1:2 EtOAc-hexane); $[\alpha]_{589}^{23}$ = +34.24° (c 0.184, MeOH); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ_H 4.33 (3H, m, 4-H & 5-H_2), 2.23 (1H, m, CH), 1.50 (9H, s, $3xCH_3$), 0.88 (3H, d, J=7.3 Hz, CH_3), 0.86 (3H, d, J=7.0 Hz, CH_3); ^{13}C-NMR ($CDCl_3$, 400 MHz) δ_C 183.9 (C=O), 148.5 (C=S), 83.7 (CMe_3), 66.6 (5-C), 62.6 (4-C), 29.6 ($CHMe_2$), 26.9 ($3xCH_3$), 17.2 (CH_3), 14.1 (CH_3); IR (KBr) ν_{max} (neat / cm^{-1}) 3109, 1812, 1722, 1368; MS (EI) *m/z* 245 (M^+, 5%), 189 ($M+H^+$ - CMe_3, 100%), 145 ($M+H^+$ - boc, 33%), 102 ($M+H^+$ - boc – $CHMe_2$, 91%), (CMe_3, 96%).

(4*S*)-4-*sec*-Butyl-2-thioxo-oxazolidine-3-carboxylic acid *tert*-butyl ester (6c): 5c (0.50 g, 3.14 mmol) was used according to the general method to afford the product as yellow oil (0.63 g, 39%); R_f 0.52 (1:2 EtOAc-hexane); $[\alpha]_{589}^{27}$ = +80.88° (c 1.36, MeOH); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ_H 4.37 (2H, m, 5-H_2), 4.09 (1H, m, 4-H), 1.46 (1H, m, CH), 1.40 (9H, s, $3xCH_3$), 1.29 (2H, m, CH_2), 0.8 (6H, m, $2xCH_3$); ^{13}C-NMR ($CDCl_3$, 400 MHz) δ_C 184.5 (C=O), 149.0 (C=S), 84.3 (CMe_3), 71.5 (5-C), 58.0 (4-C), 41.4 (CH), 27.7 ($3xCH_3$), 24.6 (CH_2), 23.5 ($CHCH_3$), 21.4 (CH_2CH_3); IR (KBr) ν_{max} (neat / cm^{-1}) 3337, 2979, 1770, 1689, 1524.

4-Methyl-2-thioxo-oxazolidine-3-carboxylic acid *tert*-butyl ester (6d): 5d (1.11 g, 9.47 mmol) was used according to the general method to afford the product as yellow solid (1.98 g, 96%) and recrystallized from EtOAc; mp: 98°C, R_f 0.58 (1:2 EtOAc-hexane); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ_H 4.60 (1H, m, 4-H), 4.53 (1H, t, J=8.5 Hz, 5-H_α), 4.15 (1H, dd, J=3.0 & 8.5 Hz, 5-H_β), 1.58 (9H, s, $C(CH_3)_3$), 1.46 (3H, d, J=6.2 Hz, CH_3); ^{13}C-NMR ($CDCl_3$, 400 MHz) δ_C 184.4 (C=O), 149.3 (C=S), 84.7 (CMe_3), 72.9 (5-C), 55.4 (4-C), 28.0 ($3xCH_3$), 19.3 (CH_3); IR (KBr) ν_{max} (neat / cm^{-1}) 2986, 1759, 1356, 1252, 1157; MS (EI) m/z 217 (M^+), 162, 144, 118, 102, 84, 57, 41.

(4*S*)-4-Methyl-2-thioxo-oxazolidine-3-carboxylic acid *tert*-butyl ester (6e): 5e (0.50 g, 4.30 mmol) was used according to the general

method to afford the product as yellow solid (0.40 g, 44%); mp: 98°C, R_f 0.60 (1:2 EtOAc-hexane); $[\alpha]_{589}^{23}$ = +73.42° (c 1.2, MeOH); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ_H 4.54 (1H, m, 4-H), 3.51 (1H, dd, J=7.4 & 11.0, 5-H_α), 2.73 (1H, d, J=11.0 Hz, 5-H_β), 1.46 (9H, s, $C(CH_3)_3$), 1.40 (3H, d, J=6.3 Hz, CH_3); ^{13}C-NMR ($CDCl_3$, 400 MHz) δ_C 170.2 (C=O), 149.1 (C=S), 83.8 (CMe_3), 55.3 (5-C), 32.2 (4-C), 28.3 (3xCH_3), 19.4 (CH_3); IR (KBr) ν_{max} (neat / cm^{-1}) 2986, 1759, 1356, 1252, 1157; MS (EI) m/z 217 (M^+), 162, 144, 118, 102, 84, 57, 41; Anal. calc. for $C_9H_{15}NO_3S$: C, 49.75; H, 6.96; N, 6.45; S, 14.76. Found: C, 50.01; H, 6.71; N, 6.36; S, 14.35%.

(1-Methyl-2-phenylsulfanyl-ethyl)-carbamic acid *tert*-butyl ester (7d): 6d (0.5 g, 2.30 mmol) was used according to the general method to afford the product as yellow oil (0.23 g, 37%); R_f 0.44 (1:4 EtOAc-hexane); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ_H 7.26 (5H, m, Ar-H_5), 4.62 (1H, br-s, NH), 3.81 (1H, m, 1-H), 3.05 (1H, dd, J=5.1 & 13.3Hz, 2-H_α), 2.83 (1H, dd, J=6.0 & 13.3Hz, 2-H_β), 1.34 (9H, s, $C(CH_3)_3$), 1.13 (1H, d, J=6.6 Hz, CH_3); ^{13}C-NMR ($CDCl_3$, 400 MHz) δ_C 155.1 (C=O), 136.4, 129.4, 129.0, 126.1, 79.3, 45.7, 40.5, 28.4, 19.9; MS (EI) m/z 267 (M^+), 211, 194, 166, 156, 150, 144, 124, 116, 109, 102, 77, 57.

((1*S*)-1-Methyl-2-phenylsulfanyl-ethyl)-carbamic acid *tert*-butyl ester (7e): 6e (0.27 g, 1.25 mmol) was used according to the general method to afford the product as yellow oil (0.23 g, 69%); R_f 0.44 (1:4 EtOAc-hexane); $[\alpha]_{589}^{31}$ = +80.44° (c 0.9, MeOH); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ_H 7.26 (5H, m, Ar-H_5), 4.62 (1H, br-s, NH), 3.81 (1H, m, 1-H), 3.05 (1H, dd, J=5.1 & 13.3Hz, 2-H_α), 2.83 (1H, dd, J=6.0 & 13.3Hz, 2-H_β), 1.34 (9H, s, $C(CH_3)_3$), 1.13 (1H, d, J=6.6 Hz, CH_3); ^{13}C-NMR ($CDCl_3$, 400 MHz) δ_C 155.1 (C=O), 136.4, 129.4, 129.0, 126.1, 79.3, 45.7, 40.5, 28.4, 19.9; IR (KBr) ν_{max} (neat / cm^{-1}) 3303, 2980, 1770, 1685, 1246; MS (EI) m/z 267 (M^+), 211, 194, 166, 156, 150, 144, 124, 116, 109, 102, 77, 57.

(2-Ethylsulfanyl-1-methyl-ethyl)-carbamic acid *tert*-butyl ester (7f): 6d (0.76 g, 3.50 mmol) was used according to the general method to afford the product as colourless oil (0.19 g, 25%); R_f 0.17 (1:2 EtOAc-hexane); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ_H 8.96 (1H, br-s, NH), 4.78 (1H, m, 1-H), 4.24 (2H, m, C*H*$_2$S), 3.55 (2H, dd, J=5.7 & 10.8Hz, 2-H_2), 1.44 (9H, s, $C(CH_3)_3$), 1.37 (1H, d, J=6.0 Hz, CH_3), 1.15 (3H, d, J=6.7Hz, C*H*$_3$CH$_2$S); ^{13}C-NMR ($CDCl_3$, 400 MHz) δ_C 157.0 (C=O), 96.9, 80.1, 77.4, 53.3, 29.3, 20.8, 18.3; MS (EI) m/z 144, 102, 88, 57, 44.

Conclusion

In this study new oxazolidinethione compounds were synthesized starting from racemic and enantiopure β-amino alcohols. Their electron-withdrawing N-*t*-boc derivatives **(6a-e)** gave nucleophilic substitution efficiency to the ring at 5-C position. A full investigation of the substitution reactions of oxazolidinethiones **(6a-e)** is now underway and will be reported later.

Besides, the synthesized oxazolidinthione compounds (**5a-e** and **6a-e**) may possess biological activity potential that is a subject of complementary research to this work.

Summary

Five new oxazolidinethiones (**5a-e**) were synthesized from the treatment of homochiral and racemic β-amino alcohols (**4a-e**) with thiophosgene. Compounds **5a-e** was protected with di-*tert*-butyl dicarbonate ((*boc*)$_2$O) to afford five new N-*boc* protected oxazolidinethiones (**6a-e**). The ring opening reactions of **6d** and **6e** at 5-C position of the oxazolidinethione heterocyclic framework gave the corresponding N-*boc* protected esters (**7d-f**). Because bonds to the asymmetric carbon were not broken in any of the synthesized compounds, the stereochemistry of these reactions all proceeded with retention of 'S' configuration. All synthesized compounds were characterized by ^{1}H NMR, ^{13}C NMR, IR and MS spectral data.

Key Words: Oxazolidinones, oxazolidinethiones, synthesis.

Özet

Yeni Oksazolidintiyonların Sentezi ve Halka Açma Tepkimeleri

Homokiral ve rasemik β-amino alkollerin (**4a-e**) tiyofosgen ile etkileştirilmesinden beş yeni oksazolidintiyon (**5a-e**) sentezlendi. **5a-e** bileşiklerinin, beş yeni oksazolidintiyon (**6a-e**) molekülü oluşturacak şekilde di-*tert*-butil dikarbonat ((*boc*)$_2$O) ile korunumları gerçekleştirildi.

6d ve **6e** oksazolidintiyon heterosiklik yapılarının 5-C pozisyonunda halka açma tepkimeleri, karşılık gelen N-boc korunumlu esterleri (**7d-f**) verdi. Reaksiyonların stereomerkeze bağlı hiçbir bağın kırılmadığı tarzda gerçekleşmesi nedeniyle, sentezlerdeki tüm tepkimelerin stereokimyası 'S' konfigürasyonun korunumuyla gerçekleşmiştir. Sentezlenmiş bileşiklerin yapıları ^{1}H NMR, ^{13}C NMR, IR ve MS spektral verilerle karakterize edildi.

Anahtar Kelimeler: Oksazolidinonlar, oksazolidintiyonlar, sentez.

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