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LETTERS TO THE EDITOR

Synthesis of New 3-Substituted 1,3-Oxazolidine-2-thiones

A. T. Takibayeva*, M. K. Ibraev, and S. K. Kabieva

Karaganda State Technical University, bulv. Mira 56, Karaganda, 100027 Kazakhstan
**e-mail: altynarai81@mail.ru*

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Abstract—Reaction of N-alkylsubstituted ethanolamines with carbon disulfide followed by reaction with benzoyl chloride afforded N-substituted oxazolidine-2-thiones.

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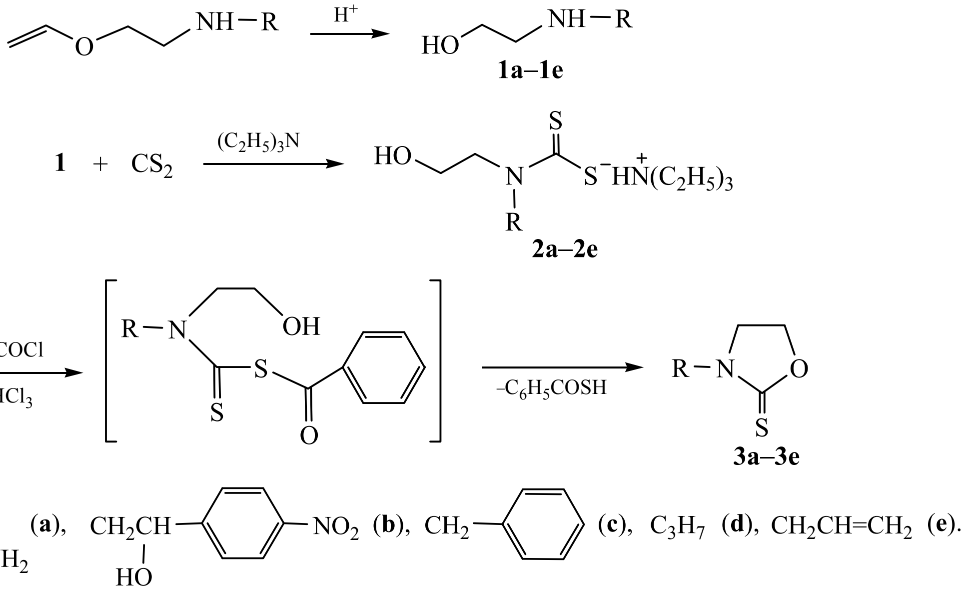
The interest to dithiocarbamates is due both to their biological activity and to the fact that they are convenient synthons for preparation of heterocyclic compounds [1–7]. In the present work, aiming at a search for new biologically active compounds, new derivatives of oxazolidine-2-thiones have been synthesized. The derivatives of oxazolidine-2-thione are known to possess valuable pharmacological properties; introduction of sulfur atom often leads to a decrease in their toxicity [8].

The reaction of N-alkylsubstituted 2-vinyloxyethanolamines **1a–1e** with carbon disulfide in the presence of triethylamine leads to dithiocarbamates **2a–2e**, which under the action of benzoyl chloride are converted to N-alkyl-substituted oxazolidine-2-thiones **3a–3e**. Compounds **3a–3e** are white crystalline solids readily soluble in polar solvents (Scheme 1).

The structure of the obtained compounds was proved by the methods of IR and NMR ^{1}H spectroscopy. In the IR spectra of compounds **3a–3e** in the range 3490–3445 cm^{-1} a wide band of ν(O–H) vibration is observed. Stretching vibrations of the NO_2 group appear at 1375–1330 cm^{-1}. In the range 1365–1325 cm^{-1} a weak absorption band of the C=S group is

Scheme 1.



present as well as ν(N–H) bands in the range 3300–3100 cm^{-1}.

The presence of two β-hydroxy groups in compound **2b** points to theoretical possibility of its cyclization by either the primary or secondary OH group. The data of ^{1}H NMR spectroscopy suggest cyclization only by the primary alcohol group, apparently, due to steric hindrances to the secondary hydroxy group created by the aryl substituent in the α-position.

***N*-(Ethanol-2-yl)aminopropionic acid amide (1a).** The solution of 1.58 g (0.01 mol) of β-2-vinyloxyethyl -aminopropionic acid amide in 20 mL of 10% sulfuric acid was stirred for 2 h at room temperature and 1 h at 40–45°C. After completionof the process, the reaction mixture was alkalinized to pH 10 and extracted with boiling benzene. The organic layer was separated, the solvent was removed. Yield 1.36 g (86%), oily compound. IR spectrum, ν, cm^{-1}: 3490 br (OH), 1375 (NO_2), 1365 (C=S), 3300 (NH). ^{1}H NMR spectrum, δ, ppm: 3.64 t (2H, $HO\underline{CH_2}CH_2N$, *J* = 5.2 Hz), 2.71 t (2H, $HOCH_2\underline{CH_2}N$, *J* = 5.2 Hz), 3.19 t (2H, $N\underline{CH_2}CH_2$, *J* = 6.72 Hz), 2.56 t (2H, $NCH_2\underline{CH_2}$, *J* = 6.59 Hz). Found, %: C 45.52; H 9.01; N 21.29. $C_5H_{12}N_2O_2$. Calculated, %: C 45.45; H 9.09; N 21.21.

2-(2-Hydroxyethylamino)-1-(4-nitrophenyl)ethanol (1b) was prepared similarly from 2.52 g (0.01 mol) of 1-(*p*-nitrophenyl)-2-vinyloxyethylaminoethanol. Yield 2.24 g (89%), white crystals. IR spectrum, ν, cm^{-1}: 3485 br (OH), 1370 (NO_2), 1360 (C=S), 3280 (NH). ^{1}H NMR spectrum, δ, ppm: 3.65 t (2H, $HO\underline{CH_2}CH_2N$, *J* = 5.2 Hz), 2.70 t (2H, $OCH_2\underline{CH_2}N$, *J* = 5.2 Hz), 2.82–2.91 m (2H, $N\underline{CH_2}CH$), 4.83 t (1H, $NCH_2\underline{CH}$, *J* = 6.8 Hz), 8.20 d (2H, *o*-CH, *J* = 8.9 Hz), 7.61 d (2H, *m*-CH, *J* = 8.9 Hz). Found, %: C 53.18; H 6.08; N 12.44. $C_{10}H_{14}N_2O_4$. Calculated, %: C 53.10; H 6.19; N 12.39.

2-Benzylaminoethanol (1c) was obtained similarly from 1.77 g (0.01 mol) of 2-vinyloxyethylbenzylamine. Yield 1.06 g (60%), oily compound. IR spectrum, ν, cm^{-1}: 3480 br (OH), 1365 (NO_2), 1355 (C=S), 3270 (NH). ^{1}H NMR spectrum, δ, ppm: 3.64 t (2H, $HO\underline{CH_2}CH_2N$, *J* = 5.2 Hz), 2.70 t (2H, $OCH_2\underline{CH_2}N$, *J* = 5.2 Hz), 7.25–7.30 m (5H, C_6H_5), 3.74 s (2H, NCH_2). Found, %: C 71.60; H 8.53; N 9.36. $C_9H_{13}NO$. Calculated, %: C 71.52; H 8.61; N 9.27.

2-Propylaminoethanol (1d) was prepared similarly from 1.29 g (0.01 mol) of 2-vonyloxyethylpropylamine. Yield 0.67 g (52%), oily compound. IR spectrum, ν, cm^{-1}: 3470 br (OH), 1355 (NO_2), 1350 (C=S), 3265 (NH). ^{1}H NMR spectrum, δ, ppm: 3.65 t (2H, $HO\underline{CH_2}CH_2N$, *J* = 5.2 Hz), 2.71 t (2H, $OCH_2\underline{CH_2}N$, *J* = 5.2 Hz), 2.67 t (2H, $N\underline{CH_2}CH_2CH_3$, *J* = 6,4 Hz), 1.46 m (2H, $NCH_2\underline{CH_2}CH_3$), 0.93 t (3H, $NCH_2CH_2\underline{CH_3}$, *J* = 5.9 Hz). Found, %: C 58.34; H 12.55; N 13.68. $C_5H_{13}NO$. Calculated, %: C 58.25; H 12.62; N 13.59.

2-Allylaminoethanol (1e) was prepared similarly from 1.26 g (0.01 mol) of 2-vinyloxyethylallylamine. Yield 0.71 g (56%), oily compound. IR spectrum, ν, cm^{-1}: 3475 ш (OH), 1360 (NO_2), 1355 (C=S), 3270 (NH). ^{1}H NMR spectrum, δ, ppm: 3.65 t (2H, $HO\underline{CH_2}CH_2N$, *J* = 5.2 Hz), 2.71 t (2H, $OCH_2\underline{CH_2}N$, *J* = 5.2 Hz), 3.46 m (2H, $N\underline{CH_2}CH{=}CH_2$), 5.82 m (1H, $NCH_2\underline{CH}{=}CH_2$), 5.07 and 5.18 d.d (1H, $NCH_2CH{=}\underline{CH_2}$, *J* = 10.2, 17.3 Hz). Found, %: C 59.48; H 10.81; N 13.94. $C_5H_{11}NO$. Calculated, %: C 59.41; H 10.89; N 13.86.

3-(2-Thioxooxazolidin-3-yl)propionamide (3a). To a solution of 1.32 g (0.01 mol) of compound **1a** and 1.01 g (0.01 mol) of triethylamine in 30 mL of benzene at 0–5°C was added dropwise a solution of 0.76 g (0.01 mol) of carbon disulfide in 10 mL of benzene. The reaction mixture was stirred at this temperature for 1 h, then 30 min at room temperature. The mixture was cooled to 0°C, the solution of 0.91 g (0.01 mol) of benzoyl chloride in 15 mL of benzene was added, and the reaction mixture was stirred with heating (60–65°C) for 2–3 h. After completion of the reaction the solvent was removed at a reduced pressure. The reaction mixture was left overnight, the precipitated crystals were filtered off and washed with benzene. Yield 3.08 g (77%), colorless crystals, mp 109–110°C. IR spectrum, ν, cm^{-1}: 3465 br (OH), 1350 (NO_2), 1345 (C=S), 3260 (NH). ^{1}H NMR spectrum, δ, ppm: 3.62 t (2H, $N\underline{CH_2}CH_2O$, *J* = 6.8 Hz), 4.12 t (2H, $NCH_2\underline{CH_2}O$, *J* = 6.7 Hz), 3.2 t (2H, $N\underline{CH_2}CH_2$, *J* = 6.7 Hz), 2.54 t (2H, $NCH_2\underline{CH_2}$, *J* = 6.6 Hz). Found, %: C 41.44; H 5.67; N 16.09. $C_6H_{10}N_2O_2S$. Calculated, %: C 41.38; H 5.75; N 16.09.

3-[1-Hydroxy-2-(4-nitrophenyl)ethyl]oxazolidine-2-thione (3b) was prepared similarly from 1.47 g (0.01 mol) of compound **1b**, 1.01 g (0.01 mol) of triethylamine, 0.76 g (0.01 mol) of carbon disulfide and 0.91 g (0.01 mol) of benzoyl chloride. Yield 2.6 g (65%), mp 115–116°C, white crystalline compound. IR spectrum, ν, cm^{-1}: 3460 br (OH), 1345 (NO_2), 1340 (C=S), 3245 (NH). ^{1}H NMR spectrum, δ, ppm: 3.62 t (2H, $N\underline{CH_2}CH_2O$, *J* = 6.8 Hz), 4.11 t (2H, $NCH_2\underline{CH_2}O$, *J* = 6.7 Hz), 2.81–2.90 m (2H, $N\underline{CH_2}CH$), 4.84 t (1H,

$NCH_2\underline{CH}$, *J* = 6.9 Hz), 8.19 d (2H, *o*-CH, *J* = 8.8 Hz), 7.62 d (2H, *m*-CH, *J* = 8.7 Hz). Found, %: C 49.32; H 4.39; N 10.45. $C_{11}H_{12}N_2O_4S$. Calculated, %: C 49.25; H 4.48; N 10.45.

3-Benzyl-1,3-oxazolidine-2-thione (3c) was prepared similarly from 1.51 g (0.01 mol) of 2-benzylaminoethanol, 1.01 g (0.01 mol) triethylamine, 0.76 g (0.01 mol) carbon disulfide and 0.91 g (0.01 mol) of benzoyl chloride. Yield 3.14 g (75%), mp 183–184°C, white crystalline compound. ИК спектр, ν, см$^{-1}$: 3455 br (OH), 1340 (NO_2), 1335 (C=S), 3225 (NH). ^{1}H NMR spectrum, δ, ppm: 3.63 t (2H, $N\underline{CH_2}CH_2O$, *J* = 6.8 Hz), 4.12 t (2H, $NCH_2\underline{CH_2}O$, *J* = 6.7 Hz), 7.23–7.27 m (5H, C_6H_5), 3.72 s (2H, NCH_2). Found, %: C 62.25; H 5.63; N 7.25. $C_{10}H_{11}NOS$. Calculated, %: C 62.18; H 5.70; N 7.25.

3-Propyl-1,3-oxazolidine-2-thione (3d) was prepared similarly from 1.03 g (0.01 mol) of 2-propylaminoethanol, 1.01 g (0.01 mol) of triethylamine, 0.76 g (0.01 mol) of carbon disulfide and 0.91 g (0.01 mol) of benzoyl chloride. Yield 2.9 g (79%), mp 179–180°C, white crystalline compound. ИК спектр, ν, cm^{-1}: 3450 br (OH), 1335 (NO_2), 1330 (C=S), 3215 (NH). ^{1}H NMR spectrum, δ, ppm: 3.60 t (2H, $N\underline{CH_2}CH_2O$, *J* = 6.8 Hz), 4.12 t (2H, $NCH_2\underline{CH_2}O$, *J* = 6.7 Hz), 2.71 t (2H, $N\underline{CH_2}CH_2CH_3$, *J* = 6.6 Hz), 1.47 m (2H, $NCH_2\underline{CH_2}CH_3$), 0.96 t (3H, $NCH_2CH_2\underline{CH_3}$, *J* = 6.1 Hz). Found, %: C 49.74; H 7.52; N 9.65. $C_6H_{11}NOS$. Calculated, %: C 49.65; H 7.59; N 9.65.

3-Allyl-1,3-oxazolidine-2-thione (3e) was prepared similarly from 1.01 g (0.01 mol) of 2-allylaminoethanol, 1.01 g (0.01 mol) of triethylamine, 0.76 g (0.01 mol) of carbon disulfide and 0.91 g (0.01 mol) of benzoyl chloride. Yield 2.4 g (65%), mp 150–151°C, white crystalline compound. IR spectrum, ν, cm^{-1}: 3445 br (OH), 1330 (NO_2), 1325 (C=S), 3100 (NH). ^{1}H NMR spectrum, δ, ppm: 3.64 t (2H, $N\underline{CH_2}CH_2O$, *J* = 6.8 Hz), 4.13 t (2H, $NCH_2\underline{CH_2}O$, *J* = 6.7 Hz), 3.46 m (2H, $N\underline{CH_2}CH{=}CH_2$), 5.82 m (1H, $NCH_2\underline{CH}{=}CH_2$), 5.07 and 5.18 d.d (1H, $NCH_2CH{=}\underline{CH_2}$, *J* = 10.0, 17.3 Hz). Found, %: C 50.43; H 6.22; N 9.79. C_6H_9NOS. Calculated, %: C 50.35; H 6.30; N 9.79.

Melting points were measured on a Boethius apparatus. IR spectra were taken on an AVATAR-320 NICOLET spectrophotometer in KBr. NMR spectra were registered on a DRX-500 spectrometer with working frequency 500 MHz in CD_3OD, internal reference TMS. The reactions were monitored and the purity of the obtained compounds controlled by the method of thin layer chromatography on Silufol UV-254 plates in the system of solvents isopropyl alcohol–ammonia–water, 7 : 2 : 1. The plates were developed with iodine vapor.

REFERENCES

1. Melnikov, N.N. and Baskakov, Yu.A., *Khimiya gerbitsidov i regulyatorov rosta rastenii* (Chemistry of Herbicides and Plant Growth Regulators), Moscow: Gos. Khim. Inst, 1962.
2. Barton, S.D. and Ollis, W.D., *Comprehensive Organic Chemistry. Phosphorus and Sulfur Compounds*, New York: Pergamon Press, 1979.
3. Busev, A.I. and Byr'ko, V.M., *Sovremennye problem i metody analiza vysokochistykh veshchestv* (Modern Problems and Methods of Analysis of High-Purity Substances), Moscow: Mir, 1972.
4. *Organicheskaya khimiya* (Organic Chemistry), Tyukavkina, N.A., Ed., Moscow: Drofa, 2002.
5. Busev, A.I., Byr'ko, V.M., and Dikusar, A.I., *Zh. Analit. Khim*., 1971, vol. 26, p. 1380.
6. Korablev, M.V., *Proizvodnye ditiokarbaminovykh kislot. Khimiya, toksikologyja, farmakologiya i klinicheskoe primenenie* (Derivatives of Dithiocarbamic Acids. Chemistry, Toxicology, Pharmacology, and Clinical Applications), Minsk: Belarus, 1971.
7. Gazaliev, A.M., Takibayeva, A.T., Ibraev, M.K., Kabieva, S.K., and Rakhimberlinova, Zh.B., *Russ. J. Gen. Chem*., 2016, vol. 86, no. 6, p. 1219. doi 10.1134/S1070363216060074
8. Kukharev, B.F., Stankevich, V.K., Lobanova, N.A., Klimenko, G.R., and Kukhareva, V.A., *Russ. J. Org. Chem*., 2005, vol. 41, no. 1, p. 103. doi 10.1007/s11178-005-0129-7