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Synthesis of 2-Sulfanylidene-1,3-thiazolidin-4-one Derivatives

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Abstract—Three-component condensation of primary amines with carbon disulfide and dialkyl maleates afforded the corresponding alkyl (3-R-4-oxo-2-sulfanylidene-1,3-thiazolidin-5-yl)acetates whose structure was confirmed by independent synthesis and IR and ^{1}H NMR spectroscopy.

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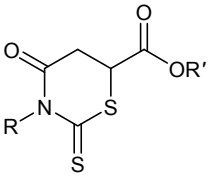
Chemistry of heterocyclic compounds is an important field of organic chemistry. Heterocycles of different nature constitute basic units of many natural and synthetic biologically active compounds possessing a broad spectrum of useful properties [1–6]. They play a significant role in biology, agriculture, pharmaceutical industry, and other fields. Therefore, studies of the synthesis of *O*,*N*,*S*-containing heterocyclic are topical, promising, and undoubtedly interesting from the theoretical and practical viewpoints.

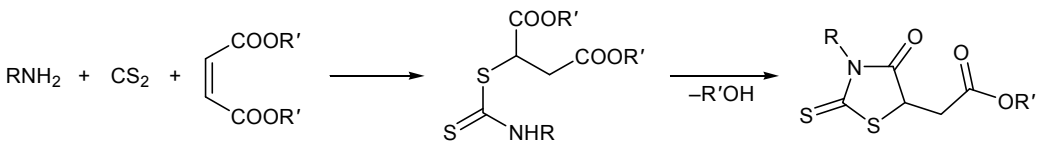
In continuation of our previous research [7, 8], it was interesting to study the three-component reaction of carbon disulfide with dialkyl maleates and primary aliphatic amines. As we found previously, this reaction gives rise to heterocyclic compounds containing a lactam moiety and a sulfur atom in the ring. It was reasonable to presume that these heterocycles are secondary products resulting from intramolecular cyclization of the primary three-component adducts **4** (Scheme 1). 2-Sulfanylidene-1,3-thiazolidin-4-one derivatives **5**–**8** were isolated as light yellow liquids readily soluble in organic solvents and synthetic oils. Their structure was confirmed by elemental analyses and IR and ^{1}H NMR spectra.

The described reaction may be expected to produce both five- and six-membered heterocycle. When the reaction was carried out at 20–80°C under atmospheric pressure in the absence of a catalyst, no six-membered heterocycle was formed. Presumably, the formation of thiazolidine ring is more favorable under these conditions. This is confirmed by the following. The reaction of allyldithiocarbamate **9** with ethyl chloroacetate (**10**) afforded thiazolidine derivative **12**, whereas intermediate linear ester **11** could not be isolated, obviously due to its fast cyclization (Scheme 2). The formation of **12** was confirmed by the IR data. It is known that the carbonyl stretching frequency for five-membered carbo- and heterocyclic compounds is higher than those for the corresponding six-membered rings [9].



The IR spectra of **5**–**8** showed strong carbonyl stretching bands in the region 1763–1745 cm^{-1}, as well as bands at 1498–1457 and 1352–1335 cm^{-1} due to the thiolactam moiety. The IR spectrum of **12** displayed absorption bands at 1757 (C=O), 1425, 1340 (NC=S), and 3088 cm^{-1} (=C–H). In the ^{1}H NMR spectrum of **12**

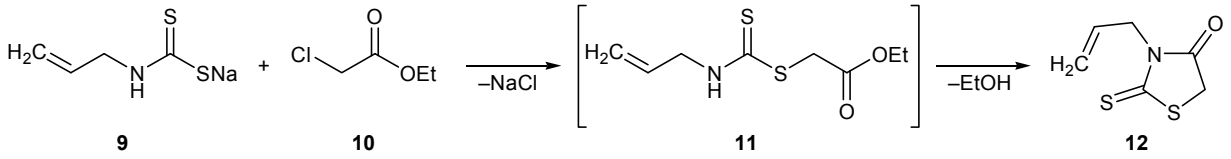
Scheme 1.



1a–1d **2** **3a–3d** **4** **5a–5d**, **6b**, **6d**, **7d**, **8d**

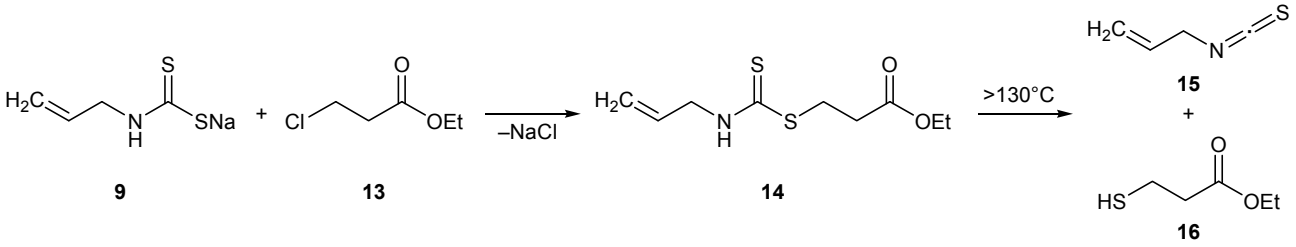
1, R = Et (**a**), *i*-Pr (**b**), Pr (**c**), CH_2=$CHCH_2$ (**d**); **3**, R′ = Me (**a**), Et (**b**), Bu (**c**), C_6H_{13} (**d**); **5**, R′ = Me, R = Et (**a**), *i*-Pr (**b**), Pr (**c**), CH_2=$CHCH_2$ (**d**); **6**, R′ = Et, R = *i*-Pr (**b**), CH_2=$CHCH_2$ (**d**); **7**, R = CH_2=$CHCH_2$, R′ = Bu (**d**); **8**, R = CH_2=$CHCH_2$, R′ = C_6H_{13} (**d**).

Scheme 2.



9 **10** **11** **12**

Scheme 3.



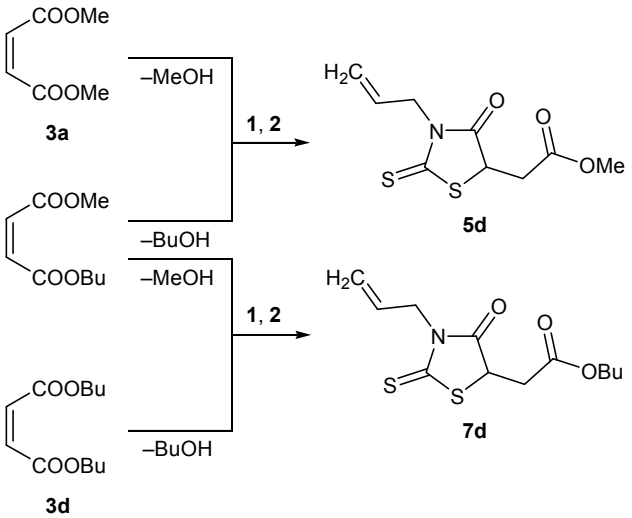
9 **13** **14** **15** **16**

we observed a doublet of the NCH_2 group at δ 4.47 ppm, a signal of the SCH_2 protons at δ 4.05 ppm, and a complex multiplet at δ 5.42 ppm due to protons of the vinyl group.

Ester **14** is a fairly stable compound; it did not undergo cyclization to six-membered heterocycle (Scheme 3). The IR spectrum of **14** showed a strong NH stretching band at about 3330 cm^{-1}. Heating of **14** to 130°C and higher resulted in its decomposition into allyl isothiocyanate (**15**) and ethyl 3-sulfanylpropanoate (**16**).

Interesting selectivity was observed in the reaction of carbon disulfide with allylamine and mixed butyl methyl maleate, which led to the formation of a mixture of methyl and butyl esters **5d** and **7d** at a ratio of 34.5:65.5 (Scheme 4). The products were identified by GC/MS and ^1H NMR using authentic samples of **5d** and **7d** which were synthesized by reactions of carbon disulfide with allylamine and dimethyl and dibutyl maleates, respectively.

Scheme 4.



3a **5d** **7d** **3d**

Thus, in the three-component reaction of carbon disulfide with allylamine and butyl methyl maleate, the dithiocarbamate residue adds preferentially to the carbon atom nearest to the methoxycarbonyl group. A probable reason is either steric factor which is significant in the electrocyclic mechanism or some difference in the electron-donor properties of the methyl and butyl groups.

EXPERIMENTAL

The IR spectra were recorded on a Specord 75 IR spectrometer. The ^1H NMR spectra were measured on a Varian T-60 spectrometer (60 MHz) using carbon tetrachloride as solvent and tetramethylsilane as internal standard.

The products were analyzed by GC/MS on a Finnigan-4021 instrument (SE-54 quartz capillary column, 30 m × 0.25 mm, film thickness 0.25 μm; sample volume 0.35 μL, split ratio 1:50; injector temperature 260°C, oven temperature 200°C; electron impact, 70 eV).

Initial sodium allylcarbamodithioate [10], butyl methyl maleate [11], and ethyl 3-chloropropanoate [12] were synthesized by known methods. Ethyl chloroacetate (**10**) and dialkyl maleates **3a**–**3d** were commercial products of analytical grade.

Compounds 5–8 (*general procedure***).** Amine **1a**–**1d**, 0.4 mmol was slowly added to a mixture of 0.4 mmol of dialkyl maleate **3a**–**3d** and 0.4 mmol of carbon disulfide, and the mixture was stirred for 1.5–2 h at 70–80°C. After cooling, the mixture was

washed with water, dried, and subjected to vacuum distillation.

Methyl (3-ethyl-2-sulfanylidene-4-oxo-1,3-thiazolidin-5-yl)acetate (5a). Yield 73.6 g (82%), mp 40–42°C. ^{1}H NMR spectrum, δ, ppm: 1.00 t (3H, CH_3, J = 9 Hz), 3.10 d (2H, 5-CH_2, J = 6 Hz), 3.74 q (3H, CH_3O), 4.00 t (1H, 5-H, J = 9 Hz), 4.50 q (2H, CH_2N). Found, %: C 41.28; H 4.60; N 6.04; S 27.34. $C_8H_{11}NO_3S_2$. Calculated, %: C 41.18; H 4.75; N 6.00; S 27.49.

Methyl [4-oxo-3-(propan-2-yl)-2-sulfanylidene-1,3-thiazolidin-5-yl]acetate (5b). Yield 79.1 g (80%), mp 72.5–73.5°C. ^{1}H NMR spectrum, δ, ppm: 1.40 d [6H, (C**H**$_3$)$_2$CH, J = 9.5 Hz], 3.10 d (2H, 5-CH_2, J = 6 Hz), 3.73 s (3H, OCH_3), 4.00 t (1H, 5-H, J = 9 Hz), 4.60 m (1H, NCH). Found, %: C 43.84; H 5.35; N 5.70; S 25.70. $C_9H_{13}NO_3S_2$. Calculated, %: C 43.70; H 5.30; N 5.66; S 25.93.

Methyl (4-oxo-3-propyl-2-sulfanylidene-1,3-thiazolidin-5-yl)acetate (5c). Yield 84.0 g (85%), bp 167–168°C (0.5 mm), d_4^{20} = 1.2640, n_D^{20} = 1.5675; MR_D = 63.96, calcd. 63.74. ^{1}H NMR spectrum, δ, ppm: 0.97 t (3H, CH_3, J = 9 Hz), 1.70 q (2H, CH_3C**H**$_2$), 3.10 d (2H, 5-CH_2, J = 6 Hz), 3.75 s (3H, CH_3O), 4.00 t (1H, 5-H, J = 9 Hz), 4.50 t (2H, NCH_2, J = 9.5 Hz). Found, %: C 43.90; H 5.70; N 5.80; S 25.76. $C_9H_{13}NO_3S_2$. Calculated, %: C 43.70; H 5.30; N 5.66; S 25.93.

Methyl [4-oxo-3-(prop-2-en-1-yl)-2-sulfanylidene-1,3-thiazolidin-5-yl]acetate (5d). Yield 73.5 g (75%), bp 161–162°C (0.5 mm), d_4^{20} = 1.2972, n_D^{20} = 1.5884; MR_D 63.67, calcd. 63.23. ^{1}H NMR spectrum, δ, ppm: 3.20 d (2H, CH_2C=O, J = 6 Hz), 3.9 t (2H, CH_2CO, J = 8.5 Hz), 4.00 t (1H, 5-H, J = 9 Hz), 4.75 m (2H, CH_2N), 5.10 d (2H, CH_2=, J = 11 Hz), 5.60 m (1H, CH=). Found, %: C 44.25; H 4.63; N 5.78; S 26.00. $C_9H_{11}NO_3S_2$. Calculated, %: C 44.06; H 4.52; N 5.71; S 26.14.

Ethyl [4-oxo-3-(propan-2-yl)-2-sulfanylidene-1,3-thiazolidin-5-yl]acetate (6b). Yield 81.5 g (78%), mp 60–61°C. ^{1}H NMR spectrum, δ, ppm: 1.10 t (3H, CH_3, J = 9 Hz), 1.40 d [6H, (C**H**$_3$)$_2$CH, J = 9 Hz), 3.10 d (2H, 5-CH_2, J = 6 Hz), 3.90 q (2H, OCH_2), 4.00 t (1H, 5-H, J = 9 Hz), 4.70 m (1H, NCH). Found, %: C 46.18; H 5.81; N 5.31; S 24.33. $C_{10}N_{15}NO_3S_2$. Calculated, %: C 45.96; H 5.78; S 24.54; N 5.36.

Ethyl [4-oxo-3-(prop-2-en-1-yl)-2-sulfanylidene-1,3-thiazolidin-5-yl]acetate (6d). Yield 78.8 g (76%), bp 162–163°C (0.3 mm), d_4^{20} = 1.2440, n_D^{20} = 1.5724; MR_D 68.63, calcd. 67.90. ^{1}H NMR spectrum, δ, ppm: 1.05 t (3H, CH_3, J = 9 Hz), 3.10 d (2H, 5-CH_2, J = 6 Hz), 3.90 q (2H, OCH_2, J = 9 Hz), 4.00 t (1H, 5-H, J = 9 Hz), 4.70 d (2H, NCH_2, J = 9.5 Hz), 5.20 d (2H, CH_2=, J = 10.5 Hz), 5.62 m (1H, CH=). Found, %: C 46.54; H 5.09; N 5.44; S 24.57. $C_{10}H_{13}NO_3S_2$. Calculated, %: C 46.31; H 5.05; N 5.40; S 24.73.

Butyl [4-oxo-3-(prop-2-en-1-yl)-2-sulfanylidene-1,3-thiazolidin-5-yl]acetate (7d). Yield 86.2 g (75%), bp 180–181°C (0.3 mm), d_4^{20} = 1.1916, n_D^{20} = 1.5579; MR_D 77.73, calcd. 77.15. ^{1}H NMR spectrum, δ, ppm: 0.90 t (3H, CH_3, J = 9 Hz), 1.20 m (4H, CH_2), 3.00 d (2H, 5-CH_2, J = 6 Hz), 3.90 t (2H, OCH_2, J = 9 Hz), 4.20 t (1H, 5-H, J = 9 Hz), 4.65 d (2H, NCH_2, J = 9 Hz), 5.30 d (2H, CH_2=, J = 10 Hz), 5.65 m (1H, CH=). Found, %: C 50.32; H 6.07; N 4.94; S 22.12. $C_{12}H_{17}NO_3S_2$. Calculated, %: C 50.15; H 6.03; N 4.87; S 22.12.

Hexyl [4-oxo-3-(prop-2-en-1-yl)-2-sulfanylidene-1,3-thiazolidin-5-yl]acetate (8d). Yield 82.0 g (65%), bp 196–197°C (0.3 mm), d_4^{20} = 1.1467, n_D^{20} = 1.5455; MR_D 87.04, calcd. 86.30. ^{1}H NMR spectrum, δ, ppm: 0.85 t (3H, CH_3, J = 9 Hz), 1.20 m [6H, $(CH_2)_4$], 3.00 d (2H, 5-CH_2, J = 6 Hz), 3.90 t (2H, OCH_2, J = 9 Hz), 4.20 t (1H, 5-CH, J = 9 Hz), 4.70 d (2H, NCH_2, J = 9 Hz), 5.30 d (2H, CH_2=, J = 10 Hz), 5.70 m (1H, CH=). Found, %: C 53.43; H 6.78; N 4.53; S 20.22. $C_{14}H_{21}NO_3S_2$. Calculated, %: C 53.30; H 6.71; N 4.44; S 20.33.

3-(Prop-2-en-1-yl)-2-sulfanylidene-1,3-thiazolidine-4-one (12). A mixture of 49.04 (0.4 mmol) of ethyl chloroacetate and 61.68 g (0.4 mmol) of sodium allylcarbamodithioate in ethanol was stirred for 4 h at 60–65°C. The mixture was cooled, washed with water, and extracted with benzene. The extract was dried over anhydrous sodium sulfate, the solvent was distilled off, and the residue was distilled under reduced pressure. Yield 68.6 g (64%), bp 121°C (0.5 mm), d_4^{20} = 1.3085, n_D^{20} = 1.6010; MR_D 47.76, calcd. 63.23. ^{1}H NMR spectrum, δ, ppm: 4.05 s (2H, 5-H), 4.47 d (2H, NCH_2, J = 8.5 Hz), 5.42 d (2H, CH_2=, J = 10.5 Hz), 5.70 m (1H, CH=). Found, %: C 41.78; H 4.10; N 8.14; S 37.24. $C_8H_{11}NO_3S_2$. Calculated, %: C 41.59; H 4.07; N 8.08; S 37.01.

Ethyl 3-{[(prop-2-en-1-yl)carbamothioyl]sulfanyl}propionate (14) was synthesized in a similar way. After cooling, the mixture was diluted with 100 mL of water and 80 mL of benzene. The benzene extract was dried over anhydrous sodium sulfate and evaporated, and the residue was distilled under reduced pressure. Yield 88%, bp 129°C (0.5 mm), d_4^{20} = 1.1445,

n_D^{20} = 1.5626; MR_D 65.47, calcd. 66.16. Found, %: C 46.65; H 6.27; N 6.52; S 27.80. $C_9H_{14}NO_2S_2$. Calculated, %: C 46.52; H 6.07; N 6.02; S 27.60.

REFERENCES

1. Novikov, R.V., Danilkina, N.A. and Balova, I.A., *Chem. Heterocycl. Compd*., 2011, vol. 47, no. 6, p. 758.
2. Mel'nikov, N.N., *Khimiya pestitsidov* (Chemistry of Pesticides), Moscow: Khimiya, 1968, p. 22.
3. Kuliev, A.M., *Khimiya i tekhnologiya prisadok k maslam i toplivam* (Chemistry and Technology of Oil and Fuel Additives), Leningrad: Khimiya, 1985, pp. 113, 124.
4. Golubev, P.R., Pankova, A.S., and Kuznetsov, M.A., *J. Org. Chem*., 2015, vol. 80, p. 4545.
5. Kulakov, I.V., Isabaeva, G.M., Nurkenov, O.A., and Fazylov, S.D., *Chem. Heterocycl. Compd*., 2009, vol. 45, no. 4, p. 498.
6. Glushkov, R.G., Levchuk, T.A., Shilova, I.B., and Gus'kova, T.A., RU Patent no. 2295958, 2007; *Byull. Izobret*., 2007, no. 9.
7. Mustafaev, N.P., Kulieva, M.A., Mustafaev, K.N., Kulibekova, T.N., Kakhramanova, G.A., Safarova, M.R., and Novotorzhina, N.N., *Russ. J. Org. Chem*., 2013, vol. 49, no. 2, p. 198.
8. Mustafaev, N.P., Efendieva, Kh.K., Akchurina, T.Kh., Novotorzhina, N.N., and Safarova, M.R., *J. Qafqaz Univ*., 2015, p. 41.
9. Bellamy, L.J., *Advances in Infra-red Group Frequencies*, London: Methuen, 1966.
10. Sletta, K.H. and Dressler, H., *Ber*., 1930, vol. 63, p. 888.
11. Gruzdev, V.G., USSR Inventor's Certificate no. 619482, 1978; *Byull. Izobret*., 1978, no. 30.
12. Mikhailova, V.N. and Pigulevskii, V.V., *Russ. J. Appl. Chem*., 1957, vol. 30, p. 1841.