Journal of the Serbian Chemical Society
JSCS-info@shd.org.rs • www.shd.org.rs/JSCS
*J. Serb. Chem. Soc.* **00(0)**S1-S6 (2025) *Supplementary material*

Accepted manuscript

SUPPLEMENTARY MATERIAL TO

# The interaction between 4-oxothiazolidine-2-ylidene thioamides and iodine: a regioselective two-component 4-oxothiazolidine-2-ylidene thioamide to thiazolo[3,2-c]pyrimidine transformation mediated by iodine

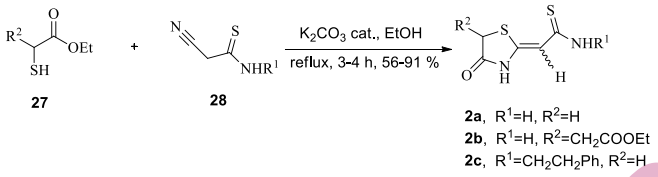
ALEKSANDAR RAŠOVIĆ

*Institute of Chemistry Technology and Metallurgy, University of Belgrade, Njegoševa 12, 11000 Beograd, Serbia.*

## SYNTHESIS, ISOLATED YIELDS, ANALYTICAL AND SPECTRAL DATA OF STARTING COMPOUNDS

*General procedure for the preparation of 4-oxothiazolidine-2-ylidine thioamides 2a-c*

The *push–pull* 2-alkylidene-4-oxothiazolidine **2a-c** derivatives were prepared according to the following general protocol previously reported[1] and slightly modified with respect to the amount of $K_2CO_3$, which was for this purpose used as the catalyst. To a suspension of the corresponding β-thioxonitrile **28** (0.01 mol) and freshly distilled α-mercaptoester (0.0172 mol; 72 % molar excess) **27** in 16 mL of ethanol, a catalytic amount of $K_2CO_3$ was added (in 4.5 mol % of the starting material) (Table 1). **CAUTION**: *All reactions involving mercapto ester, owing to the unpleasant odor, should be carried out in a well-ventilated hood*. The mixture was heated and stirred in an oil bath at 75 °C for 3–4 h when TLC indicated the accomplishment of the reaction. After that, the reaction mixture was cooled down to room temperature and the precipitated products (*E*)-**2b** and (*Z*)-**2a** were collected by filtration, washed with ethanol and recrystallized from 96 % ethanol and DMSO-water mixture (0.1 g, 7:5, v/v), respectively, to provide the final products (83–91 %). Alternatively, in the case of the preparation of (*Z*)-**2c**, the filtered solution was concentrated under reduced pressure, and the residue was chromatographed by column chromatography on silica gel (toluene/ethyl acetate, 10:0 → 1:6) affording the desired product (61 %). The structures of derivatives **2** were determined using the spectroscopic technique ($^1$H and $^{13}$C NMR)[2] and elemental analysis.




*(Z)-(4-Oxothiazolidin-2-ylidene)ethanthioamide (**2a**)*

According to the general procedure, the title compound was obtained from 1.46 g (14.6 mmol) of 2-cyanoethanthioamide, 3.02 g (25.1 mmol) of ethyl 2-mercaptoacetate and a catalytic amount of $K_2CO_3$ (0.25 g; 1.8 mmol) in ethanol (29 mL) as yellowish solid (2.31 g, 91 %). M.P.: > 240 °C (decomposes after reaching this temperature). $^1$H NMR (200 MHz, DMSO-$d_6$, $\delta$): 3.61 (s, 2H, $CH_2S$), 6.16 (s, 1H, =CH), 8.44-8.65 (d, 2H, $NH_{amide}$), 11.51 (s, 1H, $NH_{lactam}$). $^{13}$C NMR (50.3 MHz, DMSO-$d_6$, $\delta$): 32.9 ($CH_2S$), 100.6 (=CH), 158.4 (C=), 174.4 ($CO_{lactam}$), 193.2 (C=S). MS (CI): *m/z* 175 $(M+1)^+$. Combustion analysis for $C_5H_6N_2OS_2$: Calculated. C 34.46, H 3.47, N 16.08; found: C 34.84, H 3.24, N 16.02.

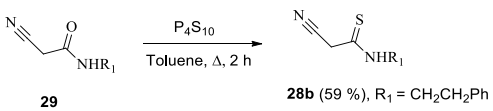
*(E)-(5-Ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)ethanthioamide (**2b**)*

According to the general procedure, the title compound was obtained from 1.20 g (12.0 mmol) of 2-cyanoethanthioamide, 4.27 g (20.7 mmol) of diethyl 2-mercaptosuccinate and a catalytic amount of $K_2CO_3$ (0.21 g; 1.5 mmol) in ethanol (19 mL) as yellow solid (2.59 g, 83 %). M.P.: 208 °C. $^1$H NMR (200 MHz, DMSO-$d_6$, $\delta$): 1.18 (t, 3H, $J$ = 7.2 Hz, $CH_3$), 3.05-3.09 (m, 2H, $CH_AH_BCOO$), 4.09 (q, 2H, $J$ = 7.2 Hz, $CH_2O$), 4.45-4.51 (m, 1H, $CH_XS$), 5.64 (s, 1H, =CH), 8.81-8.87 (d, 2H, $NH_{amide}$), 13.28 (s, 1H, $NH_{lactam}$). $^{13}$C NMR (50.3 MHz, DMSO-$d_6$, $\delta$): 14.2 ($CH_3$), 36.3 ($CH_2COO$), 41.8 ($CH_XS$), 61.0 ($CH_2O$), 97.2 (=CH), 154.9 (C=), 170.4 ($CO_{ester}$), 174.4 ($CO_{lactam}$), 191.4 (C=S). MS (CI): *m/z* 261 $(M+1)^+$. Combustion analysis for $C_9H_{12}N_2O_3S_2$: Calculated. C 41.52, H 4.65, N 10.76; found: C 41.78, H 4.42, N 10.60.

*(Z)-(4-Oxothiazolidin-2-ylidene)-N-(2-phenylethyl)ethanthioamide (**2c**)*

From 0.20 g (1.0 mmol) of 2-cyano-*N*-phenethylethanthioamide, 0.19 g (1.9 mmol) of ethyl 2-mercaptoacetate and a catalytic amount of $K_2CO_3$ (0,03 g; 0,19 mmol) in ethanol (2 mL) after column chromatography the title compound was isolated as yellowish solid (0.16 g, 61 %). M.P.: 170-172 °C. $^1$H NMR (200 MHz, DMSO-$d_6$, $\delta$): 2.86 (t, 2H, $J$ = 7.0 Hz, $CH_2Ph$), 3.62-3.73 (m, 2H, $NCH_2$), the (s, 2H, $CH_2S$) signal is overlaped with the signal assigned to the ($NCH_2$) protons, 6.21 (s, 1H, =CH), 7.16-7.35 (m, 5H, Ph), 9.58 (t, 1H, $J$ = 5.2 Hz, $NH_{amide}$), 11.51 (s, 1H, $NH_{lactam}$). $^{13}$C NMR (50.3 MHz, DMSO-$d_6$, $\delta$): 32.9 ($CH_2S$), 33.8 ($CH_2Ph$), 45.5 ($NCH_2$), 101.2 (=CH), 126.4 (*p*-Ph), 128.7 (*o*-Ph), 128.8 (*m*-Ph), 139.6 ($C_{ipso}$-Ph), 156.1 (C=), 174.3 ($CO_{lactam}$), 190.4 (C=S). MS (CI): *m/z* 279 $(M+1)^+$. Combustion analysis for $C_{13}H_{14}N_2OS_2$: Calculated. C 56.09, H 5.07, N 10.06; found: C 56.32, H 5.12, N, 9.83.

*Synthesis of 2-cyano-N-phenethylethanthioamide (**28b**)**




* As the precursor of the (*Z*)-**2a** and (*E*)-**2b**, nitrile **28a** was used as a commercial compound. On the other side, the cyano-*N*-(2-phenyl)etanthioamide **28b**, i.e., the precursor of the (*Z*)-**2c** was prepared by the below described thionation procedure.

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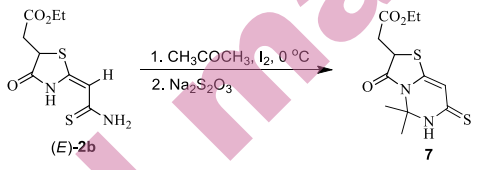
A mixture of 2-cyano-*N*-phenethylethanamide **29b** (0.70 g, 3.72 mmol) and $P_4S_{10}$ (1.24 g, 2.80 mmol) in dry toluene (30 mL) was heated in an oil bath at 75 °C. **CAUTION:** *All reactions involving phosphorous decasulfide reagent, due to the unpleasant odor, should be carried out in a well-ventilated hood*. The mixture was stirred at this temperature for an additional 3 h when TLC indicated the complete consumption of 2-cyano-*N*-phenethylethanamide **29b**. After cooling to room temperature, the heterogeneous solution was filtered and concentrated under reduced pressure. The resulting residue was chromatographed by column chromatography on silica gel (toluene/ethyl acetate, 10:0 → 7:3) affording desired product as a yellow solid in moderate yield (0.45 g, 59 %). M.P.: 93 °C. $^1$H NMR (200 MHz, DMSO-$d_6$, $\delta$): 2.89 (t, 2H, $J$ = 7.2 Hz, $CH_2Ph$), 3.69-3.76 (m, 2H, $NCH_2$), 4.03 (s, 2H, $CH_2$), 7.18-7.37 (m, 5H, Ph), 10.49 (s, 1H, $NH_{amide}$). $^{13}$C NMR (50.3 MHz, DMSO-$d_6$, $\delta$): 32.9 ($CH_2$), 34.1 ($CH_2Ph$), 47.3 ($NCH_2$), 116.7 (CN), 126.6 (*p*-Ph), 128.7 (*o*-Ph), 128.8 (*m*-Ph), 138.9 ($C_{ipso}$-Ph), 190.3 (C=S). MS (CI): *m/z* 205 $(M+1)^+$. Combustion analysis for $C_{11}H_{12}N_2S$: Calculated. C 64.67, H 5.92, N 13.71; found: C 64.47, H 5.90, N 13.52.




Yellow solid. M.P.: 145-147 °C. $^1$H NMR $^1$H NMR (200 MHz, DMSO-$d_6$, $\delta$): 1.18 (t, 3H, $J$ = 7.0 Hz, $CH_3$), 1.63 (s, 3H, $CH_3$), 1.77 (s, 3H, $CH_3$), 3.08-3.10 (m, 2H, $CH_AH_BCOO$), 4.09 (q, 2H, $J$ = 7.0 Hz, $CH_2O$), 4.50-4.55 (m, 1H, $CH_XS$), 5.73 (d, 1H, $J$ = 1.0 Hz, =CH), 9.54 (s, 1H, $NH_{lactam}$). $^{13}$C NMR (50.3 MHz, DMSO-$d_6$, $\delta$): 14.2 ($CH_3$), 25.6 ($CH_3$), 26.2 ($CH_3$), 36.1 ($CH_2COO$), 42.6 ($CH_XS$), 60.9 ($CH_2O$), 74.2 ($CNCH_3$), 101.0 (=CH), 146.8 (C=), 170.2 ($CO_{ester}$), 172.2 ($CO_{lactam}$), 184.5 (C=S). HRMS (TOF) *m/z*: calcd. for $C_{12}H_{16}N_2O_3S_2$ $[M+H]^+$: 301.06751, found: 301.06817.

*Ethyl 2-(5,5-dimethyl-3-oxo-7-thioxo-3,5,6,7-tetrahydro-2H-thiazolo[3,2-c]pyrimidin-2-yl)acetate* **7**

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SPECTRAL DATA

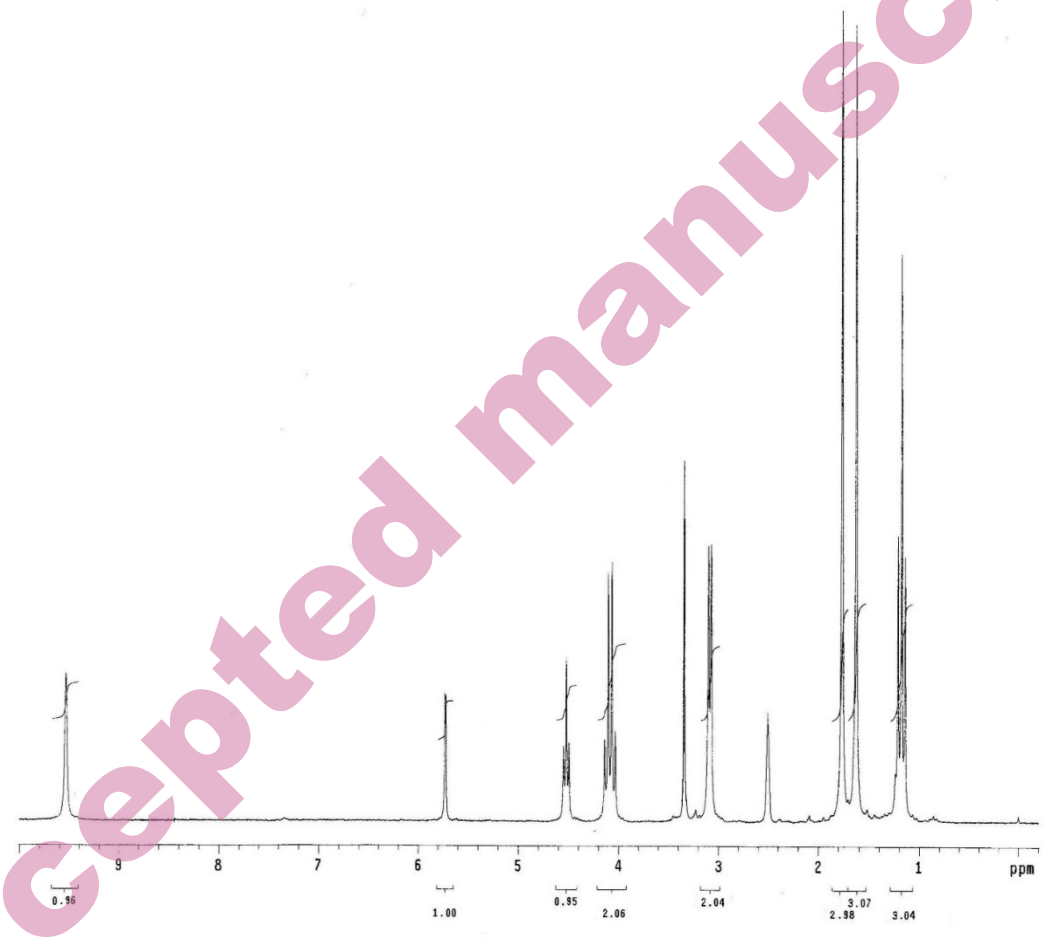


**Figure S1.** $^{1}$H NMR spectrum of the thiazolopyrimidine **7**.

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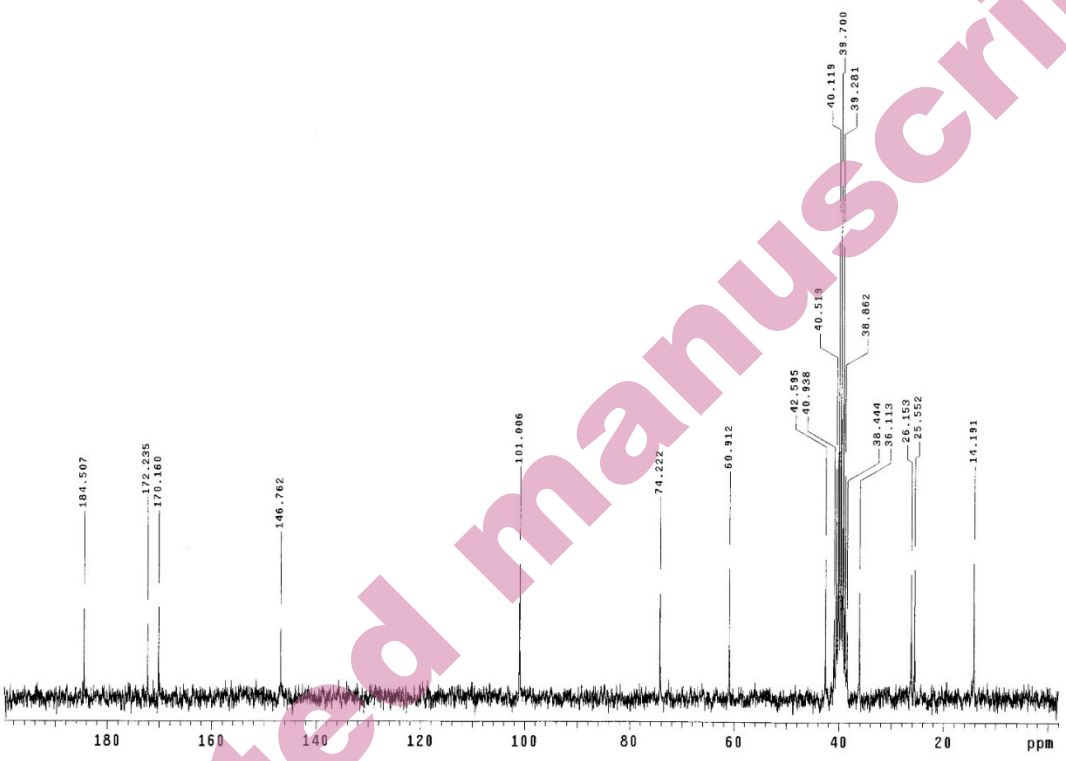


**Figure S2.** $^{13}$C NMR spectrum of the thiazolopyrimidine **7**.

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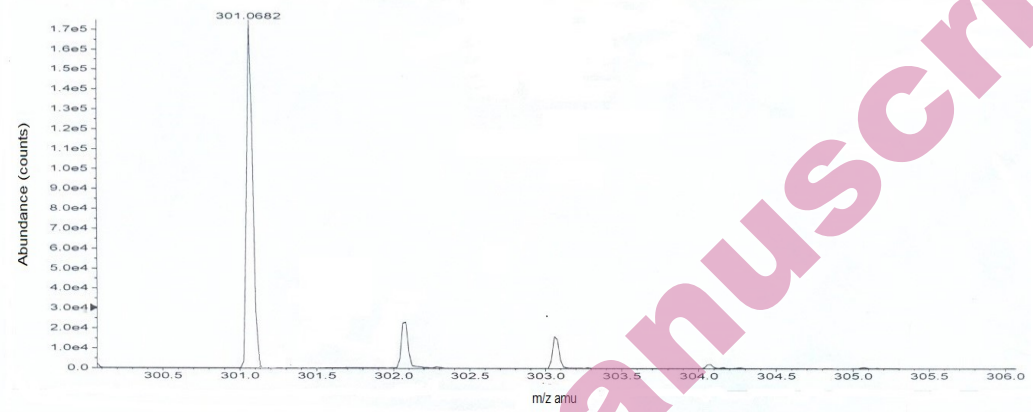


| Formula | Compound name | Mass | Peak RT (min) | Peak area | Description |
|---|---|---|---|---|---|
| C12H16N2O3S2 | -- | 300.06023 | 0.43 | 5.13012 E6 | -- |

| Species | Abundance (counts) | Ion Mass | Measured Mass | Error (mDa) | Error (ppm) | Ret. Time Error (min) |
|---|---|---|---|---|---|---|
| [M+H]+ | 176117.70 | 301.06751 | 301.06817 | 0.65630 | 2.18 | -- |

**Figure S3.** HRMS (TOF) of the thiazolopyrimidine **7**.

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2. A. Rašović, V. Blagojević, M Baranac-Stojanović, E. Kleinpeter, R. Marković, D. M. Minić, *New J. Chem.* **40** (2016) 6364 (https://doi.org/10.1039/C6NJ00901H).

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