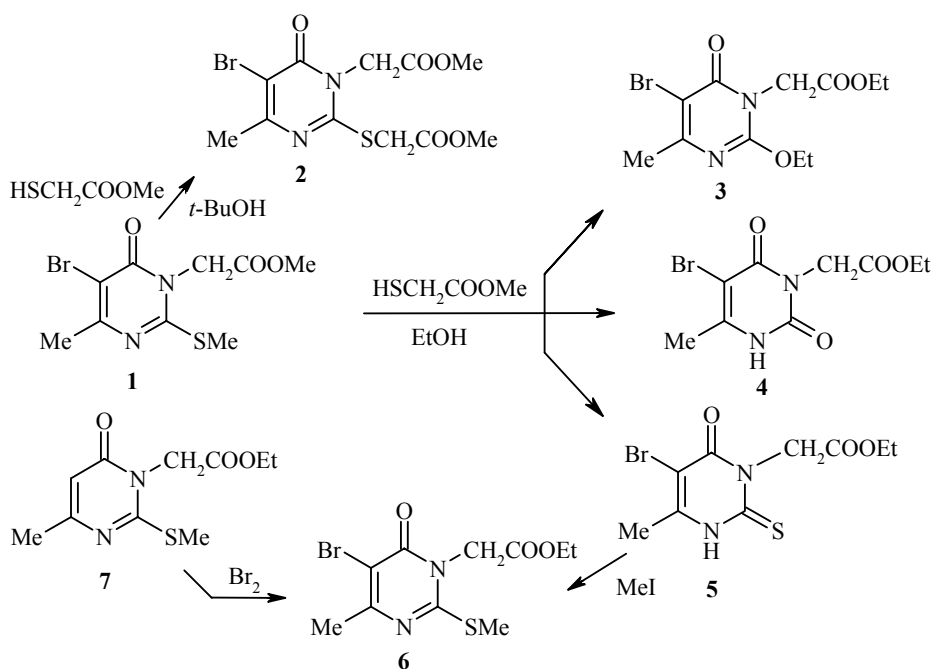


## AN UNEXPECTED CONVERSION OF METHYL (5-BROMO-6-METHYL-2-METHYLSULFANYL-4-OXO-3,4-DIHYDRO-3-PYRIMIDINYL)ACETATE ON REACTION WITH METHYL SULFANYLACETATE

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**Keywords:** 3-alkoxycarbonylmethyl-substituted uracils and 2-thiouracils, esters of (4-oxo-3,4-dihydro-3-pyrimidinyl)acetic acids.

We recently reported [1] on the possibility to synthesize compound **2** by the reaction of the corresponding 2-methylsulfanyl derivative **1** with methyl sulfanylacetate in *tert*-butanol in the presence of potassium *tert*-butoxide:



In a continuation of the search for optimal conditions for the synthesis of the diester **2**, we replaced *tert*-butanol as solvent by ethanol, and potassium *tert*-butoxide as base by potassium ethoxide. The results were very unexpected, since in this case we obtained a mixture of compounds, after isolation of which the diester **2** was

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not observed among the products. The compounds obtained appeared to be products of transesterification of the ester groups and substitution of the 2-methylsulfanyl group by ethoxy or hydroxy groups (compounds **3** and **4**) and also scission of the exocyclic S-C bond (compound **5**). The structure of the latter was confirmed by obtaining product **6** from compound **5** and the previously synthesized compound **7** [3]. We note that an analogous scission of an S-C bond in 2-alkylsulfanylpurimidines has been reported elsewhere [3].

IR spectra of KBr disks were recorded with a Perkin-Elmer BX FT-IR spectrophotometer.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of  $\text{CDCl}_3$  solutions with TMS as internal standard were recorded on a Varian Unity Inova (300 and 75 MHz respectively).

The synthesis of compound **1** was reported previously [4].

**Compounds 3-5 (General Method).** A solution of compound **1** (1.54 g, 5 mmol) in absolute ethanol (15 ml) was boiled in an atmosphere of argon for 15 min. Then a solution prepared from methyl sulfanylacetate (0.53 g, 5 mmol), sodium (0.12 g, 5 mmol), and absolute ethanol (10 ml) was added dropwise. The reaction mixture was boiled with stirring for 2h, the solvent was evaporated, the residue was dissolved in cold water and acidified to pH 4 with conc. HCl. The precipitate formed was filtered off, washed with water, and dried. A mixture of compounds (1.24 g) was obtained which was dissolved in 20:1 chloroform–ethyl acetate and separated by chromatography on silica gel (Kieselgel 60, 0.063-0.2 mm) to give compound **3** (0.124 g, 7.7%),  $R_f$  0.8 (Alugram SIL G UV<sub>254</sub>, chloroform–ethyl acetate 20:1), compound **4** (0.31 g, 21.4%),  $R_f$  0.3 (Alugram SIL G UV<sub>254</sub>, chloroform–ethyl acetate 20:1), and compound **5** (0.37 g, 24.1%),  $R_f$  0.52 (Alugram SIL G UV<sub>254</sub>, chloroform–ethyl acetate 20:1).

**Ethyl (5-Bromo-2-ethoxy-6-methyl-4-oxo-3,4-dihydro-3-pyrimidinyl)acetate (3).** Mp 75-76 °C. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1688, 1740 (C=O).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm ( $J$ , Hz): 1.32 (3H, t,  $J = 7.2$ ,  $\text{CH}_2\text{CH}_3$ ); 1.4 (3H, t,  $J = 7.2$ ,  $\text{CH}_2\text{CH}_3$ ); 2.45 (3H, s,  $\text{CH}_3$ ); 4.26 (2H, q,  $J = 7.2$ ,  $\text{CH}_2\text{CH}_3$ ); 4.48 (2H, q,  $J = 7.2$ ,  $\text{CH}_2\text{CH}_3$ ); 4.8 (2H, NCH<sub>2</sub>).  $^{13}\text{C}$  NMR spectrum,  $\delta$ , ppm: 14.3, 14.4, 25.1, 43.4, 62.1, 65.8, 104.1, 153.9, 158.9, 161.6, 167.3. Found, %: C 41.57; H 4.81; N 8.63.  $\text{C}_{11}\text{H}_{15}\text{BrN}_2\text{O}_4$ . Calculated, %: C 41.40; H 4.74; N 8.78.

**Ethyl (5-Bromo-6-methyl-2,4-dioxo-1,2,3,4-tetrahydro-3-pyrimidinyl)acetate (4).** Mp 191-192°C. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1667, 1708, 1747 (C=O), 3350 (NH).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm ( $J$ , Hz): 1.31 (3H, t,  $J = 7.2$ ,  $\text{CH}_2\text{CH}_3$ ); 2.39 (3H, s,  $\text{CH}_3$ ); 4.27 (2H, q,  $J = 7.2$ ,  $\text{CH}_2\text{CH}_3$ ); 4.74 (2H, s, NCH<sub>2</sub>); 10.67 (1H, s, NH).  $^{13}\text{C}$  NMR spectrum,  $\delta$ , ppm: 14.4, 20.5, 42.8, 62.2, 97.1, 149.3, 152, 159.1, 167.7. Found, %: C 36.98; H 4.02; N 9.85.  $\text{C}_9\text{H}_{11}\text{BrN}_2\text{O}_4$ . Calculated, %: C 37.13; H 3.81; N 9.62.

**Ethyl (5-Bromo-6-methyl-2-oxo-4-thioxo-1,2,3,4-tetrahydro-3-pyrimidinyl)acetate (5).** Mp 190-191°C. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1652, 1747 (C=O), 3214 (NH).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm ( $J$ , Hz): 1.33 (3H, t,  $J = 7.2$ ,  $\text{CH}_2\text{CH}_3$ ); 2.42 (3H, s,  $\text{CH}_3$ ); 4.28 (2H, q,  $J = 7.2$ ,  $\text{CH}_2\text{CH}_3$ ); 5.22 (2H, s, NCH<sub>2</sub>); 10.39 (1H, s, NH).  $^{13}\text{C}$  NMR spectrum,  $\delta$ , ppm: 14.4, 20.4, 48.8, 62.2, 101.6, 149.4, 157.2, 167, 175.4. Found, %: C 34.91; H 3.38; N 8.83.  $\text{C}_9\text{H}_{11}\text{BrN}_2\text{O}_3\text{S}$ . Calculated, %: C 35.19; H 3.61; N 9.12.

**Ethyl (5-Bromo-6-methyl-2-methylsulfanyl-4-oxo-3,4-dihydro-3-pyrimidinyl)acetate (6).** **A.** Compound **5** (0.31 g, 1 mmol) was added to a solution of sodium ethoxide (0.068 g, 1 mmol) in absolute ethanol (1 ml). Methyl iodide (0.14 g, 1 mmol) was added to the suspension which then was boiled with stirring for 1h, and cooled to ~ 20°C. The precipitate was filtered off and recrystallized from methanol. Yield 0.3 g (95%); mp 99-100°C.  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm ( $J$ , Hz): 1.33 (3H, t,  $J = 7.2$ ,  $\text{CH}_2\text{CH}_3$ ); 2.5 (3H, s,  $\text{CH}_3$ ); 2.63 (3H, s,  $\text{SCH}_3$ ); 4.29 (2H, q,  $J = 7.2$ ,  $\text{CH}_2\text{CH}_3$ ); 4.87 (2H, s, NCH<sub>2</sub>).  $^{13}\text{C}$  NMR spectrum,  $\delta$ , ppm: 14.4, 15.5, 25.1, 46.2, 62.5, 107.5, 158.6, 159.8, 161.4, 166.5. Found, %: C 37.6; H 4.27; N 8.78.  $\text{C}_{10}\text{H}_{13}\text{BrN}_2\text{O}_3\text{S}$ . Calculated, %: C 37.4; H 4.08; N 8.72.

**B.** Bromine (0.26 g, 1.6 mmol) was added with stirring at room temperature to a solution of compound **7** (0.24 g, 1 mmol) in glacial acetic acid (1 ml). Stirring was continued for 1 h, the precipitate was filtered off, washed with water, and recrystallized from ethanol. Yield 0.13 g (41%); mp 99-100°C.

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