

Synthesis of ethyl *N*-(6-substituted 5-cyano-2-methylthiopyrimidin-4-yl)glycinates and their cyclisation to pyrrolo[2,3-*d*]pyrimidines

Sigitas Tumkevičius,

Olegas Bobrovas and

Laura Grinciunaite

Department of Organic Chemistry,
Faculty of Chemistry, Vilnius University,
Naugarduko 24, LT-03225 Vilnius, Lithuania
E-mail: sigitas.tumkevicius@chf.vu.lt

Protection of amino groups in ethyl *N*-(6-substituted 5-cyano-2-methylthiopyrimidin-4-yl)glycinates using ethyl chloroformate, di(*tert*-butyl)dicarbonate and methylsulfonyl chloride and cyclisation of the obtained compounds to ethyl 5-amino-7*H*-pyrrolo[2,3-*d*]pyrimidine-6-carboxylates has been investigated.

Key words: *N*-(pyrimidin-4-yl)glycinates, NH protection, cyclisation, pyrrolo[2,3-*d*]pyrimidine

INTRODUCTION

Unsubstituted in the position 7 pyrrolo[2,3-*d*]pyrimidines are usually obtained by cyclisation reactions of suitably substituted pyrroles [1–3] or 6-aminopyrimidines substituted in the position 5 of the ring [4–9]. Recently it has been shown that alkyl *N*-methyl-*N*-(5-cyanopyrimidin-4-yl)glycinates in the presence of bases easily undergo cyclisation reaction to give the corresponding 7-methylpyrrolo[2,3-*d*]pyrimidines [10, 11]. However methyl group is not a suitable substituent to perform various transformations at the N7 atom of pyrrolo[2,3-*d*]pyrimidine. Therefore, synthesis of pyrrolo[2,3-*d*]pyrimidines with the unoccupied position 7 is of considerable interest in respect of further transformations and synthesis of various 7-substituted pyrrolopyrimidines. In this connection, we present herein results of a study of the protection of NH group in (pyrimidin-4-yl)glycinates and the use of the obtained compounds for synthesis of pyrrolo[2,3-*d*]pyrimidine derivatives.

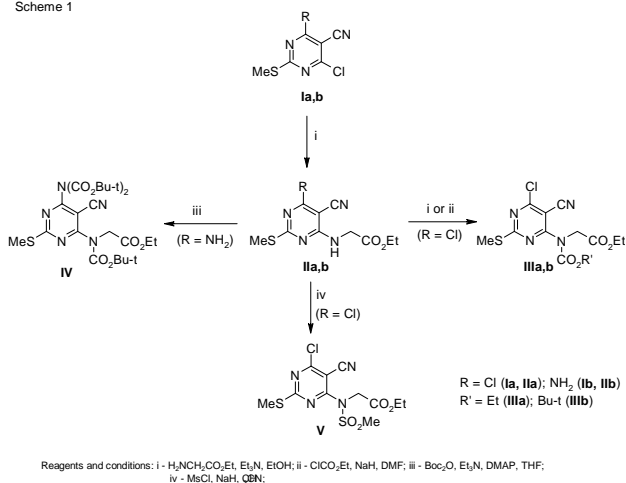
RESULTS AND DISCUSSION

Ethyl *N*-(6-substituted 5-cyano-2-methylthiopyrimidin-4-yl)glycinates (**II a, b**) were synthesised by reaction of easily obtainable 4,6-dichloro- or 6-amino-4-chloro-2-methylthiopyrimidine-5-carbonitriles (**I a, b**) [12, 13] with ethyl glycinate in the presence of triethylamine. Compounds **II a, b** when treated with sodium hydride in dimethylformamide did not give the expected pyrrolo[2,3-*d*]pyrimidines. The reason for such a behavior can be a comparatively high acidity of the NH group of a glycine moiety, because of which

sodium hydride firstly reacts with NH group to form a salt inactive in the further cyclisation reaction. In order to protect the NH group of a glycine moiety ethyl chloroformate, di(*tert*-butyl)dicarbonate (Boc₂O) and methanesulfonyl chloride (MsCl) were chosen as reagents suitable for this purpose [14]. A preliminary study of the reactivity of **IIa** towards ethyl chloroformate showed that compound **IIa** in tetrahydrofuran using pyridine, ethyldiisopropylamine or 4-dimethylaminopyridine (DMAP) as bases did not give satisfactory results: complex mixtures were formed and the target compound **IIIa** was not isolated from the reaction mixture in a pure form. Compound **IIIa** was obtained in a 31% yield when the reaction had been carried out in a mixture of tetrahydrofuran and dimethylformamide using an excess of sodium hydride (Scheme 1). Treatment of compound **IIa** with Boc₂O in tetrahydrofuran in the presence of triethylamine and DMAP led to the formation of the corresponding *N*-(*tert*-butoxycarbonyl) derivative **IIIb** in a 47% yield. Compound **IIIb** reacted with 4.5 equivalents of Boc₂O at room temperature to give compound **IV** in a 91% yield, which was pure enough to use in the subsequent reactions. Compound **V** was synthesised in a reasonable yield (60%) when the reaction of **IIa** with MsCl had been carried out in acetonitrile using a slight excess of sodium hydride.

Study of the cyclisation of compounds **III, IV** into pyrrolo[2,3-*d*]pyrimidines showed that such bases as potassium carbonate, ethyldiisopropylamine, triethylamine in dimethylformamide, tetrahydrofuran or acetonitrile caused the formation of inseparable by column chromatography mixtures. However, when an equivalent amount of sodium ethoxide in ethanol was

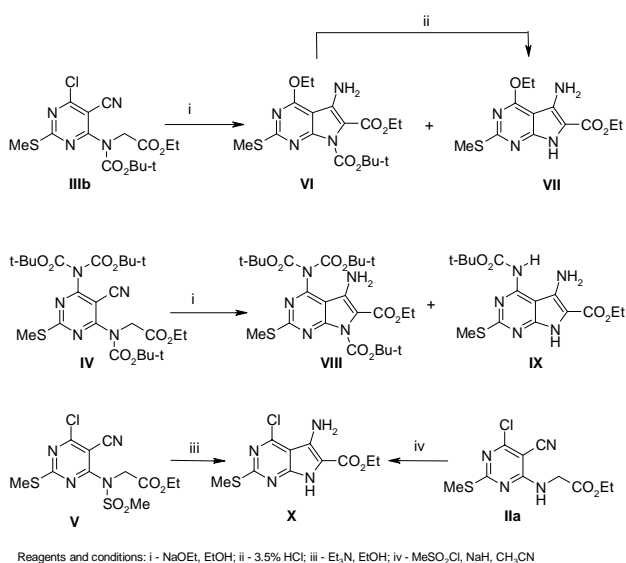
Scheme 1



used, cyclisation of **IIIb** proceeded at room temperature to form a mixture of pyrrolopyrimidines **VI** and **VII** (data of the ^1H NMR spectra) (Scheme 2). However, from the reaction mixture only compound **VI** was separated by column chromatography. In order to obtain pyrrolopyrimidine **VII**, the reaction was repeated and when the cyclisation had completed a dilute hydrochloric acid was added to remove the *tert*-butoxycarbonyl group. Compound **VII** was isolated in a 60% yield. Reaction of compound **IV** with sodium ethoxide at room temperature also proceeded with the formation of several compounds. We succeeded in isolating two compounds whose structures according to spectral and elemental analyses data corresponded to pyrrolopyrimidines **VIII**, **IX**. Heating compound **V** with triethylamine in ethanol furnished pyrrolopyrimidine **X**. In the latter reaction, removing of the methanesulfonyl group occurred together with the cyclisation reaction.

Compound **X** was also obtained by treating **IIa** with MsCl in acetonitrile in the presence of sodium hydride and subsequent work-up of the reaction mixture with water.

Scheme 2



EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were run in Nujol mulls on a Perkin-Elmer FT-IR Spectrum BX II spectrophotometer. NMR spectra were recorded on a Varian INOVA spectrometer (300 MHz) using tetramethylsilane as the internal standard. Elemental analyses were performed at the Elemental Analysis Laboratory of the Department of Organic Chemistry of Vilnius University. TLC was performed with silica gel plates 60 F₂₅₄ (Merck), visualization - UV light.

Ethyl *N*-(6-amino-5-cyano-2-methylthiopyrimidin-4-yl)glycinate (IIb). To a mixture of compound **IIb** [13] (0.44 g, 2.19 mmol), ethanol (10 ml) and ethyl ester of glycine hydrochloride (0.674 g, 4.83 mmol) triethylamine (1.343 ml, 9.64 mmol) was added dropwise. The reaction mixture was refluxed for 1 h 45 min and then cooled to room temperature. The precipitate was filtered off, washed with water and recrystallised to give 0.396 g (68%) of compound **IIb**, m.p. 225–226 °C (from EtOH). IR (cm^{-1}): 3381 (NH_2), 3119 (NH), 2204 (CN), 1724 (C = O). ^1H NMR (DMSO-d_6 , δ , ppm): 1.19 (t, 3H, $J = 7.2$ Hz, CH_3), 2.34 (s, 3H, SCH_3), 4.02 (d, 2H, $J = 5.6$ Hz, NCH_2), 4.12 (q, 2H, $J = 7.2$ Hz, OCH_2), 7.32 (s, 2H, NH_2), 7.82 (t, 1H, $J = 5.6$ Hz, NH). ^{13}C NMR (DMSO-d_6 , δ , ppm): 13.73, 14.83, 43.32, 61.09, 65.17, 116.54, 162.55, 163.93, 170.65, 173.71. Elemental analysis data: found, %: C, 45.36; H, 5.00; N, 25.88; formula $\text{C}_{10}\text{H}_{13}\text{N}_5\text{O}_2\text{S}$ (267.309): calculated, %: C, 44.93; H, 4.90; N, 26.20.

Ethyl *N*-(6-chloro-5-cyano-2-methylthiopyrimidin-4-yl)-*N*-(ethoxycarbonyl)glycinate (IIIa). A mixture of compound **IIa** [10] (0.1 g, 0.37 mmol), anhydrous dimethylformamide (2 ml) and 60% suspension of NaH (0.029 g, 0.73 mmol) in mineral oil was stirred at room temperature for 1 h under argon. The mixture was cooled to 0–5 °C and ethylchloroformate (0.053 ml, 0.55 mmol) was added dropwise. The reaction mixture was stirred for additional 1.5 h at room temperature and evaporated under reduced pressure to dryness. The residue was purified using column chromatography (eluent CHCl_3 , $R_f = 0.5$) to give 0.04 g (31%) of compound **IIIa** as an oil. IR (cm^{-1}): 2232 (CN), 1734 (C = O). ^1H NMR (CDCl_3 , δ , ppm): 1.31 (t, 3H, $J = 7.2$ Hz, CH_3), 1.39 (t, 3H, $J = 7.2$ Hz, CH_3), 2.54 (s, 3H, SCH_3), 4.25 (q, 2H, $J = 7.2$ Hz, OCH_2), 4.43 (q, 2H, $J = 7.2$ Hz, OCH_2), 4.63 (s, 2H, NCH_2). ^{13}C NMR (CDCl_3 , δ , ppm): 14.4, 14.4, 14.7, 49.5, 62.0, 64.7, 98.9, 112.8, 153.1, 162.3, 163.1, 168.4, 176.1. Elemental analysis data: found, %: C, 43.21; H, 4.27; N, 15.67; formula $\text{C}_{13}\text{H}_{15}\text{ClN}_4\text{O}_4\text{S}$ (358.801): calculated, %: C, 43.52; H, 4.21; N, 15.62.

Ethyl *N*-(*tert*-butoxycarbonyl)-*N*-(6-chloro-5-cyano-2-methylthiopyrimidin-4-yl)glycinate (IIIb). A mixture of compound **IIa** [10] (1.6 g, 5.58 mmol), anhydrous

tetrahydrofuran (20 ml), triethylamine (0.981 ml, 6.69 mmol), Boc₂O (1.536 g, 6.69 mmol) and DMAP (0.144 g, 1.12 mmol) was stirred for 30 min at room temperature. evaporated under reduced pressure to dryness. The residue was purified using column chromatography (eluent CHCl₃, R_f = 0.5) to give 1.0 g (47%) of compound **IIIb**, m.p. 115–116 °C (from ethanol). IR (cm⁻¹): 2233 (CN), 1752 cm⁻¹ (C = O). ¹H NMR (CDCl₃, δ, ppm): 1.32 (t, 3H, J = 7.2 Hz, CH₂CH₃), 1.60 (s, 9H, C(CH₃)₃), 2.53 (s, 3H, SCH₃), 4.26 (q, 2H, J = 7.2 Hz, OCH₂), 4.56 (s, 2H, NCH₂). ¹³C NMR (CDCl₃, δ, ppm): 14.5, 14.7, 28.1, 49.5, 61.9, 85.99, 99.0, 113.3, 151.4, 162.6, 162.9, 168.7, 175.9. Elemental analysis data: found, %: C, 46.54; H, 5.07; N, 14.47; formula C₁₅H₁₉ClN₄O₄S (386.5): calculated, %: C, 46.57; H, 4.95; N, 14.48.

Ethyl N-(tert-butoxycarbonyl)-N-{6-[di(tert-butoxycarbonyl)amino]-5-cyano-2-methylthiopyrimidin-4-yl}glycinate (IV). A mixture of compound **IIb** (0.1 g, 0.37 mmol), tetrahydrofuran (3 ml), Boc₂O (0.367 g, 1.68 mmol), triethylamine (0.234 ml, 1.68 mmol) and DMAP (0.018 g, 0.15 mmol) was stirred for 1 h at room temperature. Then solvents were evaporated under reduced pressure to dryness. The obtained oil was passed through a silicagel layer (eluent Et₂O:CHCl₃ = 1:1) to give 0.23 g (91%) of compound **IV**, which without further purification was used in the synthesis. IR (cm⁻¹): 2229 (CN), 1738 (C = O). ¹H NMR (CDCl₃, δ, ppm): 1.22 (t, 3H, J = 7.2 Hz, CH₃), 1.44 [s, 18H, 2 C(CH₃)₃], 1.50 [s, 9H, C(CH₃)₃], 2.42 (s, 3H, SCH₃), 4.16 (q, 2H, J = 7.2 Hz, OCH₂), 4.49 (s, 2H, NCH₂). ¹³C NMR (CDCl₃, δ, ppm): 14.4, 14.5, 28.0, 28.1, 49.5, 61.8, 85.1, 85.6, 97.3, 113.4, 149.8, 151.5, 162.1, 162.9, 168.9, 175.5.

Ethyl N-(6-chloro-5-cyano-2-methylthiopyrimidin-4-yl)-N-(methylsulfonyl)glycinate (V). To a mixture of **IIa** [10] (0.2 g, 0.7 mmol), 60% suspension of NaH (0.02 g, 0.76 mmol) in mineral oil and anhydrous acetonitrile (6 ml) was added MsCl (0.081 ml, 1.05 mmol) dropwise at 5 °C. The mixture was stirred for 15 h at room temperature. Then the temperature was increased up to 35 °C and the reaction mixture was stirred for additional 2h. The suspension was cooled to room temperature; water (10 ml) was added and extracted with diethyl ether (3*10 ml). Organic layers were combined, solvent evaporated and the product was purified using column chromatography (eluent hexane : ethyl acetate = 2:1, R_f = 0.5) to give 0.153 g (60%) of compound **V** as an oil. IR (cm⁻¹): 2225 (CN), 1749 (C = O), 1152 (SO₂). ¹H NMR (CDCl₃, δ, ppm): 1.32 (t, 3H, CH₃), 2.62 (s, 3H, SCH₃), 3.59 (s, 3H, SO₂CH₃), 4.27 (q, 2H, OCH₂), 4.96 (s, 2H, NCH₂). ¹³C NMR (CDCl₃, δ, ppm): 14.3, 14.9, 43.5, 49.5, 62.7, 95.8, 113.5, 161.3, 164.3, 168.0, 176.3.

Ethyl 5-amino-7-(tert-butoxycarbonyl)-4-ethoxy-2-methylthio-7H-pyrrolo[2,3-d]pyrimidine-6-carboxylate (VI). To a solution of sodium ethoxide, prepared from sodium (0.006 g, 0.26 mmol) and ethanol (2 ml) was

added compound **IIIb** (0.1 g, 0.26 mmol). The reaction mixture was stirred for 1 h at room temperature and evaporated under reduced pressure to dryness. The residue was purified using column chromatography (eluent CHCl₃, R_f = 0.25) to give 0.07 g (68%) of compound **VI** as an oil. IR (cm⁻¹): 3500, 3379 (NH₂), 1749 (C = O). ¹H NMR (CDCl₃, δ, ppm): 1.37 (t, 3H, J = 7.2 Hz, CH₃), 1.46 (t, 3H, J = 7.2 Hz, CH₃), 1.66 (s, 9H, Boc), 2.61 (s, 3H, SCH₃), 4.34 (q, 2H, J = 7.2 Hz, OCH₂), 4.59 (q, 2H, J = 7.2 Hz, OCH₂), 5.48 (s, 2H, NH₂). ¹³C NMR (CDCl₃, δ, ppm): 14.7, 14.8, 28.1, 60.4, 63.5, 84.4, 95.5, 103.2, 139.3, 148.6, 154.3, 162.3, 163.9, 171.4. Elemental analysis data: found, %: C, 51.74; H, 6.27; N, 14.12; formula C₁₇H₂₄N₄O₅S (396.462): calculated, %: C, 51.50; H, 6.10; N, 14.13.

Ethyl 5-amino-4-ethoxy-2-methylthio-7H-pyrrolo[2,3-d]pyrimidine-6-carboxylate (VII). To a solution of sodium ethoxide, prepared from sodium (0.006 g, 0.26 mmol) and ethanol (2 ml) was added compound **IIIb** (0.1 g, 0.26 mmol). The reaction mixture was stirred for 1 h at room temperature and evaporated under reduced pressure to dryness. The residue was dissolved in ethyl acetate or chloroform (2 ml). The obtained solution was acidified with 3.5% HCl (0.5 ml) and stirred for 1 h at room temperature. Then solvents were distilled off under reduced pressure, diethyl ether was added. The precipitate was filtered off and recrystallised to give 0.03 g (39%) of compound **VII**, m.p. 80–82 °C (from a mixture of 2-propanol-water). IR (cm⁻¹): 3492 (NH₂), 3260 (NH), 1676 (C = O). ¹H NMR (CDCl₃, δ, ppm): 1.40 (t, 3H, J = 7.2 Hz, CH₃), 1.49 (t, 3H, J = 7.2 Hz, CH₃), 2.59 (s, 3H, SCH₃), 4.38 (q, 2H, J = 7.2 Hz, OCH₂), 4.61 (q, 2H, J = 7.2 Hz, OCH₂), 5.25 (s, 2H, NH₂), 8.22 (s, 1H, NH). Elemental analysis data: found, %: C, 48.53; H, 5.25; N, 19.02; formula: C₁₂H₁₆N₄O₃S (296.35): calculated, %: C, 48.64; H, 5.44; N, 18.91.

Ethyl 5-amino-7-tert-butoxycarbonyl-4-[di(tert-butoxycarbonyl)amino]-2-methylthio-7H-pyrrolo[2,3-d]pyrimidine-6-carboxylate (VIII) and ethyl 5-amino-4-[(tert-butoxycarbonyl)amino]-2-(methylthio)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxylate (IX). A solution of compound **IV** (0.230 g, 0.34 mmol) in anhydrous ethanol (5 ml) was added to a solution of sodium ethoxide, prepared from sodium (0.016 g, 0.69 mmol) and anhydrous ethanol (2 ml). The reaction mixture was stirred for 1 h at room temperature and evaporated under reduced pressure to dryness. The residue was purified using column chromatography (eluent CHCl₃: Et₂O = 40:1) to give compound **VIII** and **IX**.

Compound **VIII**: Yield 0.022 g (11%); oil, R_f = 0.43 (CHCl₃: Et₂O/40:1). IR (cm⁻¹): 1679 (C = O), 1735 (C = O), 1759 (C = O), 3352, 3428 (NH₂). ¹H NMR (CDCl₃, δ, ppm): 1.38 (t, 3H, J = 7.2 Hz, CH₃), 1.56 [s, 9H, C(CH₃)₃], 1.67 [s, 18H, 2 C(CH₃)₃], 2.62 (s, 3H, SCH₃), 4.37 (q, 2H, J = 7.2 Hz, OCH₂), 5.89 (s, 2H, NH₂). Elemental analysis data: found,

%, C, 52.71; H, 6.62; N, 12.55; formula: $C_{25}H_{37}N_5O_8S$ (567.67); calculated, %, C, 52.90; H, 6.57; N, 12.34.

Compound **IX**: Yield 0.03 g (24%); oil, $R_f = 0.23$ ($CHCl_3$: $Et_2O/40:1$). IR (cm^{-1}): 1682 (C = O), 1725 (C = O), 3346, 3432 (NH_2). 1H NMR ($CDCl_3$, δ , ppm): 1.39 (t, 3H, $J = 7.2$ Hz, CH_3), 1.55 [s, 9H, $C(CH_3)_3$], 2.57 (s, 3H, SCH_3), 4.39 (q, 2H, $J = 7.2$ Hz, OCH_2), 5.66 (s, 2H, NH_2), 7.48 (s, 1H, NH), 8.73 (s, 1H, NH). Elemental analysis data: found, %, C, 48.83; H, 6.82; N, 19.02; formula: $C_{15}H_{21}N_5O_4S$ (367.43); calculated, %, C, 49.03; H, 6.76; N, 19.06.

Ethyl 5-amino-4-chloro-2-methylthio-7H-pyrrolo[2,3-d]pyrimidine-6-carboxylate (X). Method A. To a mixture of compound **V** (0.22 g, 0.6 mmol) and ethanol (15 ml) was added triethylamine (0.086 ml, 0.61 mmol,) dropwise. The reaction mixture was refluxed for 6 h. After cooling to room temperature solvents were evaporated under reduced pressure. The precipitate was extracted (3 · 10 ml) with hexane-ethyl acetate mixture (2:1) and purified by column chromatography (eluent hexane:ethyl acetate = 2:1). The product was recrystallised to give 0.071 g (42%) of compound **X** as a yellow solid; mp 175–177 °C (from ethanol-water). IR (cm^{-1}): 3447, 3347, 3246 (NH_2 , NH), 1671 (C = O). 1H NMR ($CDCl_3$, δ , ppm): 1.41–1.46 (t, 3H, CH_3), 2.61 (s, 3H, SCH_3), 4.39–4.46 (m, 2H, OCH_2), 5.38 (s, 2H, NH_2), 8.38 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ , ppm): 14.7, 14.8, 38.7, 60.9, 105.0, 150.2, 153.7, 154.2, 162.1, 169.7. Elemental analysis data: found, %, C, 41.82; H, 4.04; N, 19.84; formula $C_{10}H_{11}ClN_4O_2S$ (286.5): calculated, %, C, 41.89; H, 3.87; N, 19.54.

Method B. To a mixture of **IIa** (0.2 g, 0.7 mmol), anhydrous acetonitrile (6 ml), methanesulfonyl chloride (0.08 g, 0.7 mmol) was added dropwise at 0 °C. After 20 min, 60% suspension of NaH (0.03 g, 1.4 mmol) in mineral oil was added portionwise and the reaction mixture was stirred at room temperature for 24 h under argon. Then water (10 ml) was added and the mixture was extracted with chloroform (3·10 ml). Organic layers were combined, dried with Mg_2SO_4 , the solvent was evaporated and the product was purified by column chromatography to give 0.05 g (25%) of compound **X**, m.p. 175–177 °C (from ethanol-water).

CONCLUSIONS

Synthesis of ethyl *N*-alkoxycarbonyl- and *N*-methanesulphonyl-*N*-(5-cyano-2-methylthiopyrimidin-4-yl)glycinates has been accomplished. It has been found that base-promoted cyclisation reactions of the obtai-

ned compounds into the pyrrolo[2,3-*d*]pyrimidine derivatives are accompanied by deprotection reactions.

Received 06 January 2006

Accepted 12 January 2006

References

1. A. Gangjee, F. Mavandadi, S. F. Queener and J. J. McGuire, *J. Med. Chem.*, **38**, 2158 (1995).
2. A. R. Porcari and L. B. Townsend, *Synth. Commun.*, **28**, 3835 (1998).
3. R. L. Tolman, R. K. Robins and L. B. Townsend, *J. Am. Chem. Soc.*, **90**, 524 (1968).
4. A. Gangjee, R. Devraj, J. J. McGuire and R. L. Kisliuk, *J. Med. Chem.*, **38**, 4495 (1995).
5. A. Gangjee, F. Mavandadi, R. L. Kisliuk, J. J. McGuire and S. F. Queener, *J. Med. Chem.*, **39**, 4563 (1996).
6. M. Cheung, P. A. Harris and K. E. Lackey, *Tetrahedron Lett.*, **42**, 3937 (2001).
7. A. Gangjee, A. Vidwans, E. Elzein, J. J. McGuire, S. F. Queener and R. L. Kisliuk, *J. Med. Chem.*, **44**, 1993 (2001).
8. D. Edmont and D. M. Williams, *Tetrahedron Lett.*, **41**, 8581 (2000).
9. A. Gangjee, Y. Zeng, J. J. McGuire, F. Mehraein and R. L. Kisliuk, *J. Med. Chem.*, **47**, 6893 (2004).
10. S. Tumkevičius, Z. Sarakauskaitė and V. Masevičius. *Synthesis*, 1377 (2003).
11. S. Tumkevičius and Z. Sarakauskaitė, *Polish J. Chem.*, **77**, 1275 (2003).
12. A. A. Santilli, D. H. Kim and S. V. Wanser, *J. Heterocycl. Chem.*, **8**, 445 (1971).
13. D. Bellarosa, G. Antonelli, F. Bambacioni, D. Giannotti, G. Viti, R. Nannicini, A. Giachetti, F. Dianzani, M. Witvrouw, R. Pauwels, J. Desmyter and E. de Clercq, *Antiviral Res.*, **30**, 109 (1996).
14. P. J. Kocienski, *Protecting groups*, Thieme, Stuttgart-New York, 487 (2004).

Sigitas Tumkevičius, Olegas Bobrovas,
Laura Grinciūnaitė

ETIL-*N*-(4-PAKEISTŲ 5-CIAN-2-METILTIOPIRIMIDIN-4-IL)GLICINATŲ SINTEZĖ IR JŲ CIKLIZACIJOS REAKCIJOS Į PIROLO[2,3-*D*]PIRIMIDINO DARINIUS

Santrauka

Ištirtos aminogrupių blokavimo reakcijos etil-*N*-(6-pakeistuose 5-cian-2-metiltpirimidin-4-il)glicinatuose etilchlorformiatu, di(tret-butil)dikarbonatu bei metansulfonilchloridu ir susintetintų junginių ciklizacija susidarant etil-5-amino-7*H*-pirolo[2,3-*d*]pirimidin-6-karboksilatams.