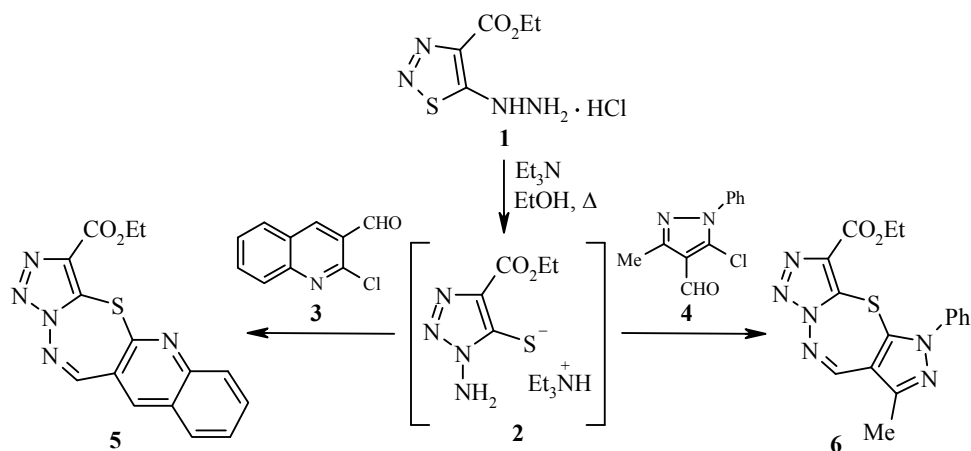


SYNTHESIS OF CONDENSED [1,2,3]TRIAZOLO- [5,1-*b*][1,3,4]THIADIAZEPINE SYSTEMS

T. A. Kalinina¹, D. V. Shatunova¹, T. V. Glukhareva¹, and Yu. Yu. Morzherin^{1*}

Keywords: pyrazoles, quinolines, 1,3,4-thiadiazepines, 1,2,3-thiadiazoles, 1,2,3-triazoles, Dimroth rearrangement.

In contemporary organic chemistry, rearrangements and transformations of one type of heterocycle to another are promising and convenient methods for the preparation of heterocyclic structures difficult to obtain by other means. However, these reactions are rarely used as a planned method for preparing heterocyclic systems. 1,2,3-Thiadiazoles are convenient starting materials for carrying out various rearrangements. Several rearrangements of 1,2,3-thiadiazoles involving a substituent in the ring position 5 are known [1-3], but only a few of these lead to the preparation of condensed 1,2,3-triazoles. Thus, for example, methods are known for the synthesis of [1,2,3]triazolo[5,1-*b*][1,3,4]thiadiazepines using the Dimroth rearrangement [4, 5].



We propose a method for the preparation of novel condensed [1,2,3]triazolo[5,1-*b*][1,3,4]thiadiazepines from the 5-hydrazino-1,2,3-thiadiazole **1**. The first stage of this process is a Dimroth rearrangement of the 5-hydrazino-1,2,3-thiadiazole **1** [4] in ethanol in the presence of triethylamine. The subsequent stage is a cyclocondensation of the intermediate 5-mercapto-1,2,3-triazoles **2** (without their separation from the reaction mixture) with the quinoline **3** [6] or pyrazole **4** [7] derivatives, which contain chlorine and formyl groups at the *ortho* position.

*To whom correspondence should be addressed, e-mail: yu.yu.morzherin@ustu.ru.

¹Ural Federal University named after the First President of Russia B. N. Yeltsin, 19 Mira St., Yekaterinburg 620002, Russia.

The resultant [1,2,3]triazolo[5',1':2,3][1,3,4]thiadiazepino[7,6-*b*]quinoline **5** and 7-methyl-5-phenyl-5*H*-pyrazolo[4,3-*f*][1,2,3]triazolo[5,1-*b*][1,3,4]thiadiazepine **6** have not been reported before in the literature. Similar condensed quinolino- [8-10] and pyrazolothiadiazepines [11] were prepared from 1-amino-5-mercapto-1,3,4-triazole.

Thus, we have proposed a one-pot method for the synthesis of tri- and tetracyclic triazolothiadiazepines.

The ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance-II 400 spectrometer (400 and 100 MHz, respectively) using DMSO- d_6 with TMS as internal standard. Mass spectra were recorded on a Finnigan MAT 8200 spectrometer at an ionization potential of 70 eV and with direct introduction of the sample into the source. Elemental analysis was performed on a PE 2400 Series II CHNS-analyzer. Melting points were determined using a Stuart SMP3 heating apparatus. Monitoring of the reaction course and the purity of the synthesized materials was performed by TLC on Silufol UV-254 plates with ethyl acetate–hexane (1:2) mobile phase.

Condensed Ethyl [1,2,3]Triazolo[5,1-*b*][1,3,4]thiadiazepine-3-carboxylates **5**, **6** (General Method).

Et_3N (0.45 ml, 4.46 mmol) was added to a suspension of ethyl 5-hydrazino-1,2,3-thiadiazole-4-carboxylate hydrochloride **1** (0.5 g, 2.23 mmol) in ethanol (20 ml) and heated to dissolution. The aldehyde **3** or **4** (2.23 mmol) was then added; the reaction mixture was refluxed for 3 h, cooled, and the precipitate formed was filtered off. The product was recrystallized from ethanol.

Ethyl [1,2,3]Triazolo[5',1':2,3][1,3,4]thiadiazepino[7,6-*b*]quinoline-3-carboxylate (5). Yield 0.42 g (58%). Mp 236-238°C. ^1H NMR spectrum, δ , ppm (J , Hz): 1.16 (3H, t, $J = 7.0$, OCH_2CH_3); 4.16 (2H, q, $J = 7.0$, OCH_2CH_3); 7.55-7.61 (2H, m, H Ar); 7.74 (1H, dd, $J = 7.2$, $J = 8.8$, H Ar); 8.01 (1H, d, $J = 8.0$, H Ar); 8.88 (1H, s, H-11); 9.19 (1H, s, H Ar). ^{13}C NMR spectrum, δ , ppm: 13.6; 60.2; 124.9; 125.2; 127.0; 127.7; 128.6; 129.8; 132.2; 140.0; 142.0; 142.1; 146.9; 153.9; 160.0. Mass spectrum, m/z (I_{rel} , %): 325 $[\text{M}]^+$ (7), 281 $[\text{M-OEt}]^+$ (30), 224 (54), 153 (100), 140 (54), 126 (49), 113 (33), 101 (52), 76 (17), 69 (49). Found, %: C 54.98; H 3.46; N 21.51; S 9.69. $\text{C}_{15}\text{H}_{11}\text{N}_5\text{O}_2\text{S}$. Calculated, %: C 55.38; H 3.41; N 21.53; S 9.86.

Ethyl 7-Methyl-5-phenyl-5*H*-pyrazolo[4,3-*f*][1,2,3]triazolo[5,1-*b*][1,3,4]thiadiazepine-3-carboxylate (6). Yield 0.15 g (66%). Mp 210-212°C. ^1H NMR spectrum, δ , ppm (J , Hz): 1.26 (3H, t, $J = 7.0$, OCH_2CH_3); 2.39 (3H, s, CH_3); 4.28 (2H, q, $J = 7.0$, OCH_2CH_3); 7.56-7.86 (5H, m, H Ph); 8.54 (1H, s, H-8). ^{13}C NMR spectrum, δ , ppm: 12.2; 14.3; 61.6; 115.9; 125.1; 125.5; 129.7; 129.9; 134.8; 136.2; 137.4; 151.8; 153.0; 159.5. Mass spectrum, m/z (I_{rel} , %): 354 $[\text{M}]^+$ (6), 281 $[\text{M-OEt}]^+$ (1), 253 (90), 225 (45), 215 (22), 185 (28), 159 (24), 128 (27), 77 $[\text{Ph}]^+$ (100), 69 (33). Found, %: C 54.17; H 4.04; N 23.51; S 9.03. $\text{C}_{16}\text{H}_{14}\text{N}_6\text{O}_2\text{S}$. Calculated, %: C 54.23; H 3.98; N 23.71; S 9.05.

This work was carried out with the financial support of the Russian Foundation for Basic Research (grant 13-03-00137).

REFERENCES

1. Yu. Yu. Morzherin, T. V. Glukhareva, and V. A. Bakulev, *Khim. Geterotsikl. Soedin.*, 803 (2003). [*Chem. Heterocycl. Compd.*, **39**, 679 (2003)].
2. A. A. Shchipalkin, M. L. Petrov, and V. A. Kuznetsov, *Zh. Org. Khim.*, **47**, 1191 (2011). [*Russ. J. Org. Chem.*, **47**, 1209 (2011)].
3. T. A. Kalinina, P. E. Prokhorova, T. V. Glukhareva, and Yu. Yu. Morzherin, *Izv. Akad. Nauk, Ser. Khim.*, 957 (2011). [*Russ. Chem. Bull., Int. Ed.*, **60**, 981 (2011)].
4. G. L'Abbé and E. Vanderstede, *J. Heterocycl. Chem.*, **26**, 1811 (1989).
5. Y. Y. Morzherin, T. V. Glukhareva, I. N. Slepukhina, V. S. Mokrushin, A. V. Tkachev, and V. A. Bakulev, *Mendeleev Commun.*, **10**, 19 (2000).
6. O. Meth-Cohn and D. L. Taylor, *Tetrahedron*, **47**, 12869 (1995).

7. B. Datterl, N. Tröstner, D. Kucharski, and W. Holzer, *Molecules*, **15**, 6106 (2010).
8. B. Prabhuswamy and S. Y. Ambekar, *Synth. Commun.*, **29**, 3487 (1999).
9. J. J. Vora, D. R. Patel, N. V. Bhimani, and P. V. Ajudia, *J. Chil. Chem. Soc.*, **56**, 771 (2011).
10. B. Kalluraya, R. Gururaja, and G. Rai, *Indian J. Chem., Sect. B*, **42**, 211 (2003).
11. M. Gupta, S. Paul, and R. Gupta, *Indian J. Chem., Sect. B*, **48**, 460 (2009).