Chemistry of Heterocyclic Compounds, Vol. 32, No. 2, 1996

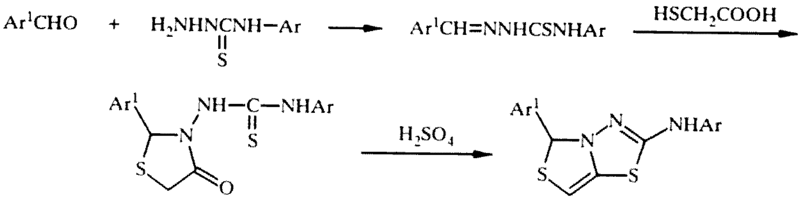
NEW REACTION OF THIONOHYDRAZIDES WITH SEMITHIOACETALS OF THIOGLYCOLIC ACID. ONE-STEP SYNTHESIS OF 2-R-THIO-5-R-5H-THIAZOLO[4,3-b]-1,3,4-THIADIAZOLES

S. Sh. Shukurov, M. A. Kukaniev, A. M. Alibaeva,
and B. M. Bobogaribov

It was found that aromatic aldehydes, thioglycolic acid and thionohydrazides (methyldithiocarbazate) in equimolar proportions at room temperature in concentrated sulfuric acid are converted into 2-methylthio-5-R-5H-thiazolo[4,3-b]-1,3,4-thiadiazoles.

Continuing our studies of the synthesis of 2-R-thio-1,3,4-thiadiazoles and their condensed analogs [1-6], we found the synthetic paths leading to 2-R-thio-5-R-5H-thiazolo[4,3-b]-1,3,4-thiadiazoles (Ia-d).

The existing method of constructing this heterocyclic system is based on the reaction of thionohydrazides with aldehydes with the formation of hydrazones and their subsequent conversion, under action of thioglycolic acid, into amino-substituted 3-amino-2-R-4-oxo-1,3-thiazolidines. Acid dehydration of the latter in concentrated H_2SO_4 leads to the stated objective [7-10]. In this way, 2-amino(arylamino)-5-R-5H-thiazolo[4,3-b]-1,3,4-thiadiazoles were prepared.



The method in question involves three steps and requires separation of the reaction intermediates.

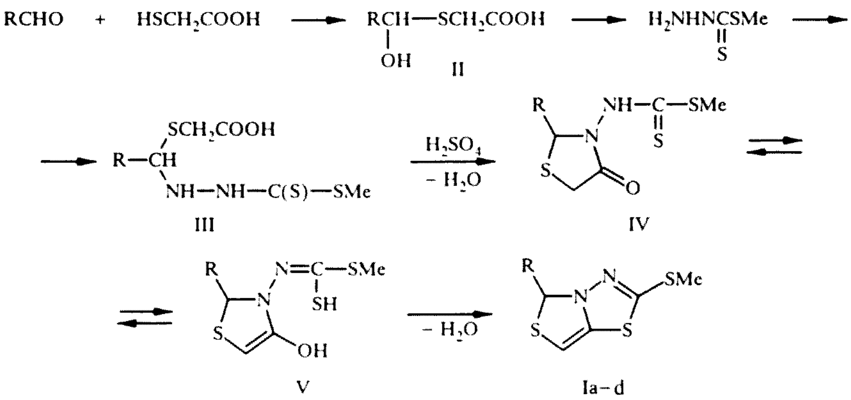
We have proposed a one-step synthesis of the indicated heterocyclic system by use of thionohydrazides, thioglycolic acid, and aromatic aldehydes in concentrated H_2SO_4 at room temperature. We observed that the most acceptable method was the preliminary conversion of aromatic aldehydes to the semithioacetals, carried out by mixing equimolar amounts of the components. In view of exothermicity of the reaction, the forming semithioacetal of thioglycolic acid II, without separation from the reaction mixture, can spontaneously react with thionohydrazides with conversion to hydrazidothioesters III. Adding conc. H_2SO_4 to the reaction mixture and letting the latter stand at room temperature for 10-18 h results in the formation of 2-R-thio-5-Ar-5H-thiazolo[4,3-b]-1,3,4-thiadiazoles (Ia-d).

The intermediate compound III, acted upon by H_2SO_4, probably dehydrates to the methyl ester of N-(2-Ar-4-oxothiazolidin-3-yl)dithiocarbamic acid IV, which after conversion to the enol form V dehydrates and converts into the final product Ia-d. Apart from the main product Ia-d, we were unable to isolate any other secondary compounds, although during

---

V. I. Nikitin Institute of Chemistry, Republic of Tadzhikistan, Dushanbe 734063. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 271-273, February, 1996. Original article submitted December 1, 1995.

0009-3122/96/3202-0243$15.00 ©1996 Plenum Publishing Corporation



I a R = Ph, b R = $C_6H_4NO_2$-*p*, c R = C_6H_4F-*p*, d R = 2-HO-5-BrC_6H_3

cyclization we observed the evolution of sulfur dioxide. This indicates that in addition to its dehydrating effect, sulfuric acid also has an oxidizing effect.

Compounds Ia-d are crystalline substances which dissolve well in many organic solvents.

The IR spectra of Ia-d lack the absorption bands in the 1630-1680 cm^{-1} region which are characteristic of the stretching vibrations of the carbonyl group of compound III; this confirms the thiazolo[4,3-b]-1,3,4-thiadiazole structure. The 2850-3150 cm^{-1} region has three absorption bands due to the stretching vibrations of the aromatic-ring CH group. The spectra show (C–C) bands of variable intensity at 1600 cm^{-1}, which can be attributed to the normal vibrations of the aromatic ring. In the 1600-500 cm^{-1} interval, the spectra showed the presence of a series of bands whose appearance is probably due to the 5-phenyl-5H-thiazolo[4,3-b]-1,3,4-thiadiazole skeleton. In the ESR spectra, the signals of the thiomethyl-group protons were recorded as a singlet at 2.26-2.43 ppm. The signals of the methine proton and proton in the 5 position of the hydrothiazole ring are manifested at 13.04-13.4 ppm and 8.21-8.38 ppm, respectively. The resonance lines of the phenyl-ring protons are observed at 6.51-8.38 ppm.

EXPERIMENTAL

The IR spectra were recorded in KBr pellets with a UR-20 spectrometer, and the ESR spectra were recorded with a Tesla 587-C instrument at a frequency of 80 MHz (in DMSO-D_6), HMDS being used as the internal standard. The melting point was determined on a Boetius microheater table.

General method of preparation of 2-methylthio-5-R-5H-thiazolo[4,3-b]-1,3,4-thiadiazoles (Ia-d). The aromatic aldehyde in the amount of 11 mmole is mixed with 11 mmole of thioglycolic acid for 5-10 min, then 10 mmole of methyldithiocarbazate is added in portions. After 30-40 min, the mixture is transferred to an ice bath, 10 ml of conc. H_2SO_4 is added in portions, and the mixture is allowed to stand for 10-18 h. It is then diluted with a 3 to 4-fold excess of water, and the precipitate of Ia-d is filtered off and washed with water until the reaction is neutral. The product is dried in air and recrystallized from isopropanol.

2-Methylthio-5-phenyl-5H-thiazolo[4,3-b]-1,3,4-thiadiazole (Ia). IR spectrum: 3130, 2985, 2870, 1610, 1525, 1490, 1330, 1305, 1105, 1045, 965, 875, 760, 690, 670, 610, 532 cm^{-1}. ESR spectrum: 2.41 (3H, s, Me), 7.40 (5H, m, Ar), 7.63 (5H, m, Ar), 8.21 (H, s, CH), 13.4 ppm (H, s, CH). Yield, 1.9 g (71.4%), mp 155-157°C. Found, %: N 10.38. $C_{11}H_{10}N_2S_3$. Calculated, %: N 10.52.

2-Methylthio-5-(4-nitrophenyl)-5H-thiazolo[4,3-b]-1,3,4-thiadiazole (Ib). IR spectrum: 3090, 3000, 2920, 1615, 1535 (Ar–NO), 1510, 1350 (Ar–NO), 1300, 1120, 1055, 960, 810, 740, 700, 680, 620, 540 cm^{-1}. ESR spectrum: 2.43 (3H, s, Me), 7.64-8.18 (4H, m, Ar), 8.23 (H, s, CH), 13.18 ppm (H, s, CH). Yield, 2.7 g (87%), mp 198-201°C. Found, %: N 13.23. $C_{11}H_9N_3O_2S_3$. Calculated, %: N 13.49.

2-Methylthio-5-(4-fluorophenyl)-5H-thiazolo[4,3-b]-1,3,4-thiadiazole (Ic). IR spectrum: 3130, 2985, 2870, 1610, 1510, 1335, 1300, 1235, 1160, 1110, 1040, 965, 830, 645, 525, 505 cm^{-1}. ESR spectrum: 2.42 (3H, s, Me), 7.18 (2H, m, Ar), 7.70 (2H, m, Ar), 8.20 (H, s, CH), 11.21 ppm (H, s, CH). Yield, 2.05 g (72.2%), mp 175-177°C. Found, %: N 9.72. $C_{11}H_9FN_2S_3$. Calculated, %: N 9.85.

2-Methylthio-5-(2-hydroxy-5-bromophenyl)-5H-thiazolo[4,3-b]-1,3,4-thiadiazole (Id). IR spectrum: 3620 (OH), 3110, 2980, 2860, 1620, 1530, 1483, 1330, 1300, 1270 (ArO), 1190 (ArO), 1055, 925, 810, 645, 530 cm^{-1}. ESR spectrum: 2.26 (3H, s, Me), 6.60 (H, d, Ar), 7.14 (H, q, Ar), 7.52 (H, d, Ar), 8.22 (H, s, CH), 13.10 ppm (H, s, CH). Yield, 3 g (82%), mp 204-205°C. Found, %: N 7.90. $C_{11}H_9BrN_2OS_3$. Calculated, %: N 7.75.

The authors are grateful to Prof. L. I. Belen'kii for his assistance in the preparation of the paper for press.

REFERENCES

1. S. Sh. Shukurov and M. A. Kukaniev, Zh. Org. Khim., **29**, 2327 (1993).
2. S. Sh. Shukurov and M. A. Kukaniev, Khim. Geterotsikl. Soedin., No. 8, 1148 (1992).
3. S. Sh. Shukurov and M. A. Kukaniev, Khim. Geterotsikl. Soedin., No. 1, 139 (1993).
4. S. Sh. Shukurov and M. A. Kukaniev, Izv. Akad. Nauk Ser. Khim., 231 (1993).
5. S. Sh. Shukurov, M. A. Kukaniev, V. M. Bobogaribov, and S. S. Sabirov, Khim. Geterotsikl. Soedin., No. 8, 1145 (1993).
6. S. Sh. Shukurov, M. A. Kukaniev, V. M. Bobogaribov, and S. S. Sabirov, Khim. Geterotsikl. Soedin., No. 8, 1146 (1993).
7. H. Singh, L. D. S. Yadav, and J. P. Chandhary, J. Indian Chem. Soc., **60**, 768 (1983).
8. L. D. S. Yadov, A. Vaish, and S. Sharma, J. Agr. Food Chem., **42**, No. 3, 811 (1994); Ref. Zh. Khim., 24Zh334 (1994).
9. B. E. Bayoumy, J. Serb. Chem. Soc., **55**, 205 [sic].
10. B. E. Bayoumy and G. Skulski, Bull. Pol. Acad. Sci. Chem., **39**, 449 (1991).