# Reactions of 2-aminothiophenol with pyridine- and imidazolecarboxaldehydes*

*E. S. Barskaya, E. K. Beloglazkina,* A. G. Mazhuga, I. V. Yudin, and N. V. Zyk*

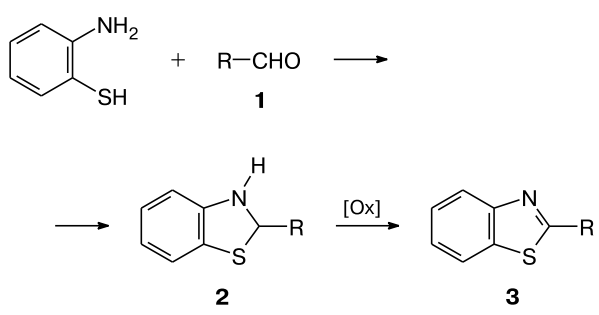
*Chemistry Department, M. V. Lomonosov Moscow State University,*
*1/3 Leninskie Gory, 119991 Moscow, Russian Federation.*
*E-mail: bel@org.chem.msu.ru*

Reflux of imidazole-2-carboxaldehyde, 1-methylimidazole-2-carboxaldehyde, imidazole-4-carboxaldehyde, or 5-bromopyridine-2-carboxaldehyde with 2-aminothiophenol in ethanol in the presence of air oxygen for 1.5 h affords the corresponding 2-hetaryl-substituted 1,3-benzothiazoles. The reaction of 2-(1-methyl-1*H*-imidazol-2-yl)-1,3-benzothiazole with $Cu(ClO_4)_2 \cdot 6H_2O$ gives bis[2-(1-methyl-1*H*-imidazol-2-yl)-1,3-benzothiazole]copper(II) diperchlorate monohydrate.

**Key words:** benzothiazoles, 2-pyridinecarboxaldehyde, imidazolecarboxaldehyde, copper(II) complex.

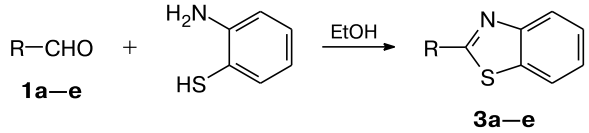
It is known that reactions of condensation of aldehydes **1** with 2-aminothiophenol can afford organic products of two types (Scheme 1): 1,3-benzothiazolines **2** (see Refs 1—7) and products of their oxidative aromatization, 1,3-benzothiazoles **3**.[8—11] Benzothiazolines **2** are often oxidized to benzothiazoles **3** with air oxygen in the course of the reaction or during isolation from the reaction mixture.[12] There are literature data that substituent R in position 2 of benzothiazoline (see Scheme 1) plays the key role in the determination of the oxidation rate, since the oxidation occurs, as a rule, much more rapidly at R = aryl, furyl, pyrrolyl, and thienyl that in the case of R = 2-Py. On the basis of the data of quantum chemical calculations and X-ray diffraction analysis, the authors explained[13] this fact by the presence of the N—H(thiazoline)···N(pyridyl) hydrogen bond that impedes oxidation with hydrogen atom detachment from the nitrogen atom of the thiazoline cycle.

**Scheme 1**




To check this hypothesis, we studied the reactions of various imidazole- (**1a—c**) and pyridinecarboxaldehydes (**1d**,**e**) with 2-aminothiophenol in ethanol in the presence of air oxygen. In all cases, formed 2-hetarylbenzothiazolines contain the donor nitrogen atom in the α-position of the heterocycle and, hence, can form a hydrogen bond with the benzothiazoline fragment. It was found that the corresponding 2-hetarylbenzothiazoles **3a—e** were formed as reaction products in the yields from 39 to 93% in all cases (Scheme 2). Note that assumed benzothiazolines **2** were not isolated as reaction products even when the reaction was carried out under argon in a degassed solvent: it is most likely that the oxidation to benzothiazole **3** occurs, in this case, when the reaction mixture is filtered and the product is dried in air.

**Scheme 2**




| 1, 3 | R | Yield of 3 (%) |
|---|---|---|
| a | Imidazol-2-yl | 47 |
| b | 1-Methylimidazol-2-yl | 52 |
| c | Imidazol-4-yl | 39 |
| d | Pyridin-2-yl | 93 |
| e | 5-Bromopyridin-2-yl | 68 |

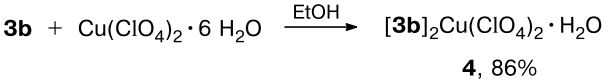
To additionally confirm the structures of the obtained compounds, we synthesized copper-containing complex **3b** by the reaction of this benzothiazole with copper(II) perchlorate hexahydrate. It is known that in the reactions with bivalent metal complexes 2-hetarylbenzothiazoles

* Based on the materials of the XXVI International Chugaev Conference on Coordination Chemistry (October 6—10, 2014, Kazan, Russia).

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 8, pp. 1975—1977, August, 2015.

form metal complexes containing one or two initial organic ligands coordinated to the corresponding metal ion,[14—18] whereas 2-hetarylbenzothiazolines undergo benzothiazoline ring opening to form tautomeric iminothiophenol, the reaction of which with $M^{2+}$ gives the corresponding bis(ligand) iminothiolate complex.[18—25] The reaction of imidazole-substituted benzothiazole **3b** with $Cu(ClO_4)_2 \cdot 6H_2O$ affords copper complex **4** having, according to the elemental analysis data, empirical formula $L_2Cu(ClO_4)_2 \cdot H_2O$ similarly to the earlier synthesized[17] coordination compound of $Cu^{II}$ with 2-(2-pyridyl)benzothiazole **1d** (Scheme 3).

**Scheme 3**




Thus, we found that for all 2-hetarylcarboxaldehydes studied the reaction with 2-aminothiophenol affords 2-hetarylbenzothiazoles **3** rather than 2-benzothiazolines **2**, as it could be expected on the basis of published data.[13] It is most likely that the hypothesis proposed earlier[13] about the key role of the electrostatic interaction between the heterocyclic N atom and the NH group of the benzothiazoline fragment in the determination of the rate of the oxidation of the latter to benzothiazole is insufficient for the unambiguous prediction of the result of the reaction of 2-aminothiophenol with heteroaromatic aldehydes.

## Experimental

The reaction course was monitored by thin-layer chromatography in the fixed silica gel layer (Silufol plates). $^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker Avance instrument with working frequencies of 400 and 100 MHz. IR spectra were measured on a UR-20 instrument in Nujol. Aldehydes **1a—e** and 2-aminothiophenol (Aldrich) were used without additional purification. 2-(Pyridin-2-yl)-1,3-benzothiazole **3d** (m.p. 132—133 °C) was synthesized according to described procedure[8] (Ref. 8: m.p. 130 °C).

**Reaction of 2-aminothiophenol with hetarylcarboxaldehydes (general procedure).** One—two droplets of glacial acetic acid were added to a mixture of 2-aminothiophenol (1 equiv.) and imidazole- or pyridinecarboxaldehyde (1 equiv.) in ethanol. The reaction mixture was refluxed with stirring for 1.5 h. The precipitate formed after cooling was filtered off and dried in air.

**2-(1*H*-Imidazol-2-yl)-1,3-benzothiazole (3a).** The reaction of 2-aminothiophenol (0.6 mL, 5 mmol) and 1*H*-imidazole-2-carboxaldehyde (0.48 g, 5 mmol) in EtOH (15 mL) gave compound **3a** (0.49 g, 47%) as a black powder, m.p. 185 °C. $^1H$ NMR (DMSO-$d_6$), δ: 13.5 (s, 1 H, NH); 8.15 (d, 1 H, $J$ = 7.4 Hz); 8.02 (d, 1 H, $J$ = 8.2 Hz); 7.65 (t, 1 H, $J$ = 8.2 Hz); 7.47 (t, 1 H, $J$ = 8.2 Hz); 7.42 (s, 1 H); 7.18 (s, 1 H). $^{13}C$ NMR (DMSO-$d_6$), δ: 153.97, 139.85, 134.37, 129.80, 126.97, 126.95, 126.10, 123.33, 122.52. IR, ν/cm$^{-1}$: 1575. Found (%): C, 59.92; H, 3.71; N, 20.79, S, 15.68. $C_{10}H_7N_3S$. Calculated (%): C, 59.68; H, 3.51; N, 20.88; S, 15.93.

**2-(1-Methyl-1*H*-imidazol-2-yl)-1,3-benzothiazole (3b).** The reaction of 2-aminothiophenol (0.56 mL, 4.65 mmol) and 1-methyl-1*H*-imidazole-2-carboxaldehyde (0.51 g, 4.65 mmol) in EtOH (15 mL) gave compound **3b** (0.52 g, 52%) as a brown powder, m.p. 133—135 °C (Ref. 26: m.p. 134—136 °C). $^1H$ NMR (DMSO-$d_6$), δ: 8.10 (d, 1 H, $J$ = 8.0 Hz); 8.05 (d, 1 H, $J$ = 8.0 Hz); 7.55 (t, 1 H, $J$ = 7.2 Hz); 7.50 (s, 1 H); 7.46 (т, 1 H, $J$ = 7.2 Hz); 7.15 (s, 1 H); 4.20 (s, 3 H). $^{13}C$ NMR (DMSO-$d_6$), δ: 156.28, 153.66, 152.30, 144.85, 141.09, 134.62, 131.10, 127.07, 125.97, 122.86, 35.87. IR, ν/cm$^{-1}$: 1610. Found (%): C, 61.36; H, 4.18; N, 19.33; S, 15.13. $C_{11}H_9N_3S$. Calculated (%): C, 61.37; H, 4.21; N, 19.52; S, 14.89.

**2-(1*H*-Imidazol-4-yl)-1,3-benzothiazole (3c).** The reaction of 2-aminothiophenol (0.6 mL, 5 mmol) and 1*H*-imidazole-2-carboxaldehyde (0.48 g, 5 mmol) in EtOH (15 mL) gave compound **3c** (0.375 g, 39%), m.p.. 166—168 °C (Ref. 27: m.p. 136 °C). $^1H$ NMR (DMSO-$d_6$), δ: 8.05 (d, 1 H, $J$ = 7.1 Hz); 7.93 (s, 1 H); 7.88 (d, 1 H, $J$ = 7.1 Hz); 7.83 (s, 1 H); 7.45 (t, 1 H, $J$ = 7.1 Hz); 7.33 (t, 1 H, $J$ = 7.1 Hz). $^{13}C$ NMR (DMSO-$d_6$), δ: 172.43, 154.25, 150.15, 135.82, 131.54, 126.54, 124.86, 122.47, 116.49, 115.22. IR, ν/cm$^{-1}$: 1577. Found (%): C, 59.38; H, 4.04; N, 20.75, S, 15.78. $C_{10}H_7N_3S$. Calculated (%): C, 59.68; H, 3.51; N, 20.88; S, 15.93.

**2-(5-Bromopyridin-2-yl)-1,3-benzothiazole (3e).** The reaction of 2-aminothiophenol (0.42 mL, 3.4 mmol) and 5-bromo-2-pyridinecarboxaldehyde (0.63 g, 3.4 mmol) in EtOH (10 mL) gave compound **10** (0.68 g, 68%) as a white powder, m.p. 212 °C. $^1H$ NMR (DMSO-$d_6$), δ: 8.75 (d, 1 H, $J$ = 8.2 Hz); 8.53 (d, 1 H, $J$ = 2.2 Hz); 8.12 (d, 1 H, $J$ = 8.2 Hz); 8.3 (t, 1 H, $J$ = 8.1 Hz); 7.97 (d, 1 H, $J$ = 7.9 Hz); 7.55 (d, 1 H, $J$ = 7.1 Hz); 7.45 (t, 1 H, $J$ = 7.2 Hz). $^{13}C$ NMR (DMSO-$d_6$), δ: 153.89, 150.76, 149.72, 139.67, 136.02, 126.5, 125.94, 123.54, 122.58, 122.02, 121.91, 102.79. IR, ν/cm$^{-1}$: 1575. Found (%): C, 49.54; H, 2.59; N, 9.69; S, 11.07. $C_{12}H_7BrN_2S$. Calculated (%): C, 49.50; H, 2.42; N, 9.62; S, 11.01.

**Bis[2-(1-methyl-1*H*-imidazol-2-yl)-1,3-benzothiazole]copper(II) diperchlorate monohydrate (4).** A solution of benzothiazole **3b** (0.11 g, 0.51 mmol) and $Cu(ClO_4)_2 \cdot 6H_2O$ (0.095 g, 0.26 mmol) in EtOH (10 mL) was refluxed for 1 h and cooled. The formed green precipitate was filtered off and dried in air. Compound **4** was obtained in a yield of 0.159 g (86%), m.p. > 250 °C. IR, ν/cm$^{-1}$: 3380 (br), 1565. Found (%): C, 37.23; H, 2.88; N, 11.60, S, 9.62. $C_{22}H_{18}Cl_2CuN_6O_8S_2 \cdot H_2O$. Calculated (%): C, 37.16; H, 2.84; N, 11.82, S, 9.02.

This work was financially supported by the Russian Foundation for Basic Research (Project No. 13-03-00399-a).

## References

1. R. C. Elderfield, E. C. McClenachan, *J. Am. Chem. Soc.*, 1960, **82**, 1982.
2. M. T. Bogert, B. Naiman, *J. Am. Chem. Soc.*, 1935, **57**, 1529.
3. S. Ratner, H. T. Clarke, *J. Am. Chem. Soc.*, 1937, **59**, 200.
4. F. J. Kreysa, V. F. Maturi, J. J. Finn, J. J. McClarnon, F. Lombardo, *J. Am. Chem. Soc.*, 1951, **73**, 1155.
5. K. Meenakshi, P. Kumar, S. Kumar, *Pharma Chemica*, 2011, **3**, 213.

6. M. Sebastian, V. Arun, P. P. Robinson, K. Yusuff, K. Mohammed, *Synthesis and Reactivity in Inorganic*, *Metal-Organic*, *and Nano-Metal Chemistry,* 2010, **40**, 541.
7. E. K. Beloglazkina, A. G. Majouga, I. V. Yudin, R. D. Rakhimov, B. N. Tarasevich, S. V. Zatonsky, N. V. Zyk, *J. Sulfur Chem.*, 2007, **28**, 201.
8. N. Kundu, A. Audhya, S. M. T. Abtab, S. Ghosh, E. R. T. Tiekink, M. Chaudhury, *Cryst. Growth Des.*, 2010, **10**, 1269.
9. K. Yamamoto, M. Fujita, K. Tabashi, Y. Kawashima, E. Kato, M. Oya, T. Iso, J. Iwao, *J. Med. Chem.*, 1988, **31**, 919.
10. Y. Huang, H. Gan, S. Li, J. Xu, X. Wu, H. Yao, *Tetrahedron*, 2010, **51**, 1751.
11. T. Itoh, K. Nagata, H. Ishikawa, A. Ohsawa, *Heterocycles*, 2004, **63**, 2769.
12. H. P. Lankelma, P. X. Sharnoff, *J. Am. Chem. Soc.*, 1931, **53**, 2654.
13. M. A. Lynn, L. J. Carlson, H. Hwangbo, J. M. Tanski, L. A. Tyler, *J. Mol. Struct.*, 2012, **1011**, 81.
14. Y. Lu, Y. Chen, Z. Ou, S. Chen, C. Zhuang, X. Le, *Chin. J. Chem.,* 2012, **30**, 303.
15. P. U. Maheswari, M. van der Ster, S. Smulders, S. Barends, G. P. van Wezel, C. Massera, S. Roy, H. den Dulk, P. Gamez, J. Reedijk, *Inorg. Chem.*, 2008, **47**, 3719.
16. J. L. Corbin, D. E. Work, *Can. J. Chem.*, 1974, **52**, 1054.
17. E. K. Beloglazkina, A. G. Majouga, I. V. Yudin, A. A. Moiseeva, A. I. Tursina, N. V. Zyk, *Russ. Chem. Bull.* (*Int. Ed.*), 2006, **55**, 1803 [*Izv. Akad. Nauk*, *Ser. Khim.*, 2006, 1738].
18. L. J. Carlson, J. Welby, K. A. Zebrowski, M. M. Wilk, R. Giroux, N. Ciancio, J. M. Tanski, A. Bradley, L. A. Tyler, *Inorg. Chim. Acta*, 2011, **365**, 159.
19. V. C. Ezeh, A. K. Patra, T. C. Harrop, *Inorg. Chem.*, 2010, **49**, 2586.
20. H. A. Tayim, A. S. Salameh, *Polyhedron*, 1983, **2**, 1091.
21. C. J. Jones, J. A. McCleverty, *J. Chem. Soc. A*, 1971, **12**, 37.
22. A. S. Salameh, H. A. Tayim, B. C. Uff, *Polyhedron*, 1982, **6**, 543.
23. A. C. Braithwaite, C. E. F. Rickard, T. N. Waters, *Inorg. Chim. Acta*, 1978, **26**, 63.
24. K. Singh, R. Singh, J. P. Tandon, *Bull. Chem. Soc. Jpn*, 1988, **61**, 4494.
25. A. C. Braithwaite, C. E. F. Rickard, T. N. Waters, *Transition Met. Chem.*, 1975, **1**, 5.
26. W. Han, P. Mayer, A.R. Ofial, *Angew. Chem., Int. Ed.*, 2011, **50**, 2178.
27. S. Das, S. Samanta, S. K. Maji, P. K. Samanta, A. K. Dutta, D. N. Srivastava, B. Adhikary, P. Biswas, *Tetrahedron Lett.*, 2013, **54**, 1090.

*Received December 3, 2014;*
*in revised form February 27, 2015*