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SYNTHESIS OF BENZO[*b*]THIENO-[3,2-*e*]BENZIMIDAZOLES, FIRST REPRESENTATIVES OF A NEW HETEROCYCLIC SYSTEM

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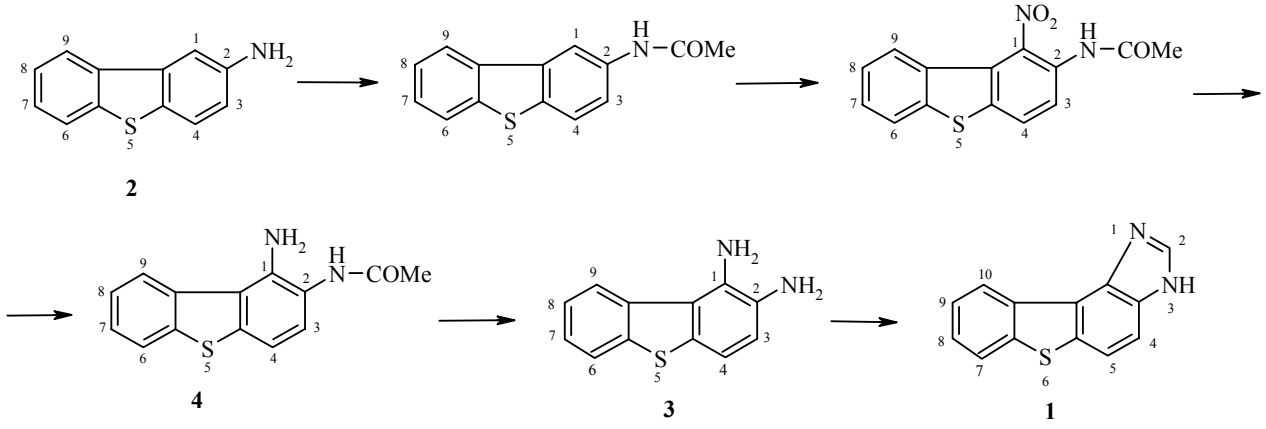
In the present work, we have prepared a tetracyclic condensed system containing bicyclic benzo[*b*]thiophene and benzimidazole fragments, each of which separately has high pharmacological activity. The idea to combine these fragments was based on the high activity of imidazole derivatives, of which *dibasol*, antibiotic *azomycin* (2-nitroimidazole) [2, 3], and histidine (an amino acid) [4] form an incomplete list of pharmaceuticals used in medicine. We have synthesized unsubstituted benzo[*b*]thieno[3,2-*e*]benzimidazole (**1**), which is first representative of a new heterocyclic system.



2-Aminodibenzothiophene (**2**) [1] was selected as the starting compound. A series of transformations converted this compound into 1,2-diaminodibenzothiophene **3**, which gives unsubstituted 1H-benzo[*b*]thieno-[3,2-*e*]benz-imidazole (**1**) by the action of formic acid in the presence of a catalytic amount of concentrated hydrochloric acid.

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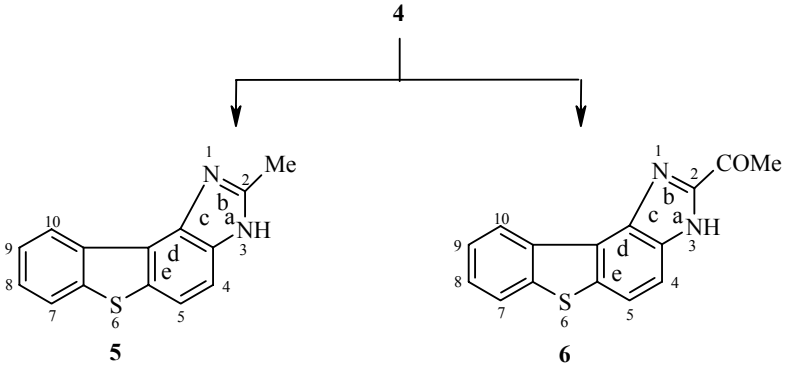
The cyclization of 2-acetylamino derivative **4** gave 2-substituted benzothieno-benzimidazoles **5** and **6**, which will permit study of the biological activity of 1H-benzo[*b*]thieno-[3,2-*e*]benzimidazole derivatives. Carrying out the cyclization in formic or acetic acid in the presence of ethyl orthoformate and a catalytic amount of hydrochloric acid gives 2-acetylbenzo[*b*]thieno[3,2-*e*]benzimidazole (**6**). The cyclization in acetic acid catalyzed by hydrochloric acid without ethyl orthoformate leads to 2-methylbenzo[*b*]thieno-[3,2-*e*]benzimidazole (**5**). The structures of these compounds were established by ^{1}H NMR and IR spectroscopy.



5 **6**

The course of the reactions and purity of the products were monitored on Silufol UV-254 plates using 1:3:5 benzene–ethyl acetate–ether as the eluent. The IR spectra were taken on a UR-20 spectrometer with NaCl and LiF prisms for vaseline mulls. The ^{1}H NMR spectra were taken on a Bruker WP 20SY spectrometer at 200 MHz in DMSO–d_6 with TMS as the internal standard.

Benzo[*b*]thieno[3,2-*e*]benzimidazole (1). A mixture of 1,2-diaminodibenzothiophene (10.7 g, 0.05 mol), formic acid (3.48 ml), and concentrated hydrochloric acid (1 ml) was heated at reflux for 1.5-2 h in a 100 ml three-necked flask. Then, activated charcoal (1 g) was added and the mixture was heated at reflux for an additional 15-20 min. The charcoal was filtered off. The filtrate was carefully made basic with vigorous stirring and cooling by adding dilute ammonium hydroxide until a slight odor of ammonia was detected. The precipitate formed was filtered off, thoroughly washed with four portions of glacial acetic acid (25 ml), and dried to give compound **1** in 80% yield; mp 236-238°C. IR spectrum, ν, cm^{-1}: 1670 (C=O), 3360 (NH), 1560 (imidazole ring). ^{1}H NMR spectrum, δ, ppm: 12.80 (1H, br. s, NH); 9.01 (1H, m, CH); 8.39 (1H, s, CH); 8.04 (1H, m, CH); 7.75 (2H, s, CH); 7.60 (2H, m, CH). Found, %: C 69.5; H 3.6; N 12.7; S 14.5. $C_{13}H_8N_2S$. Calculated, %: C 69.65; H 3.57; N 12.50; S 14.28.

1H-2-Methylbenzo[*b*]thieno[3,2-*e*]benzimidazole (5). A mixture of 2-acetylamino-1-aminodibenzo-thiophene (**4**) (0.5 g, 1.9 mmol), acetic acid or formic acid (7 ml), and concentrated hydrochloric acid (1-2 ml) was stirred for 40 min at 60°C. At the end of the reaction, the flask contents were cooled to room temperature and made basic by adding dilute ammonium hydroxide. The crystalline precipitate was filtered off and washed with water until the wash water was neutral. A white powder was formed in quantitative yield. Recrystallization from benzene gave compound **5** in 80% yield, mp 248-250°C, R_f 0.21. IR spectrum, ν, cm^{-1}: 3300 (NH); 1550 (imidazole ring). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 12.60 (1H, br. s, NH); 8.97 (1H, m, CH); 8.01 (1H, m, CH); 7.71 (1H, d, J_o = 8.1, CH); 7.62 (1H, d, J_o = 8.1, CH); 7.50 (2H, m, CH); 2.64 (3H, s, CH_3). Found, %: C 79.7; H 4.5; N 11.7; S 13.0. $C_{14}H_{10}N_2S$. Calculated, %: C 70.58; H 4.20; N 11.76; S 13.44.

2-Acetyl-1H-benzo[*b*]thieno[3,2-*e*]benzimidazole (6). A mixture of compound **4** (0.5 g, 1.7 mmol), ethyl orthoformate (1.5 ml), and formic acid (5 ml) with two drops of hydrochloric acid was stirred for 30-35 min at 60°C. After cooling, dilute ammonium hydroxide was added until the mixture was basic. The

crystalline precipitate was filtered off, washed with water, and dried to give compound **6** in quantitative yield. Recrystallization from benzene gave 2.8 g (85%) compound **6**; mp 243-245°C, R_f 0.18. IR spectrum, ν, cm^{-1}: 1670 (C=O); 3360 (NH); 1560 (imidazole ring). ^1H NMR spectrum, δ, ppm (*J*, Hz): 12.60 (1H, s, NH); 9.17 (1H, m, CH); 8.14 (1H, m, CH); 8.11 (1H, d, J_o = 8.8, CH); 7.86 (1H, d, J_o = 8.8, CH); 7.60 (2H, m, CH); 2.96 (3H, s, $COCH_3$). Found, %: C 70.5; H 4.6; N 11.9; S 13.7. $C_{14}H_{10}N_2S$. Calculated, %: C 70.58; H 4.20; N 11.76; S 13.44.

REFERENCES

1. H. Gilman and G. R. Wilder, *J. Am. Chem. Soc.*, **76**, 2906 (1954).
2. A. F. Pozharskii, Yu. D. Garnovskii, and A. M. Simonov, *Usp. Khim.*, **45**, 269 (1966).
3. R. Elderfield, *Heterocyclic Compounds* [Russian translation], vol. 5, Izd. Inos. Lit., Moscow (1961), p. 161.
4. M. D. Mashkovskii, *Drugs* [in Russian], Meditsina, Moscow, part 2 (1993), p. 114.