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## Novel diazole and dibenzothiophenedioxide containing tetracyclic systems with promising biological activities

**Abstract:** The aim of the current work is to create new heterocyclic pentacyclic condensed systems which combine benzothiofen and benzimidazole/triazole into one molecule.

As the original mixture we have dibenzothiofene and imidazole and triazole nucleus are annulated in consistent "extension" way. In result we have two new tetracyclic systems: 3H-imidazole[4,5-b]di-benzothiophene-5,5dioxide and 3H-imidazole[4,5-a]dibenzothiophene-5,5dioxide with the promising antimicrobial activity. Their spectral characteristics are studied.

**Keywords:** Dibenzothiophendioxide, Imidazole, Tetracyclic systems

### 1. Introduction

Huge amount of pathogenic and conditionally pathogenic micro-organisms strains are characterized by both genetic and acquired resistance to anti-microbial drugs are being changing periodically. It is highly important to know identified physiologically active molecule chemical modification to get the new drugs, which also means combining biologically active molecules into one molecule that often leads to changes of biological activeness intensity and/or changes in spectrum.

Biologically active mixture synthesis with heterocyclic combination base is one of the main directions of learning new medicines. Strategic covers: combination of biologically active heterocycles, such as imidazole and dibenzothiofene in one molecule; adding different pharmacophoric substitutes into adoption of derivatives; and learning the physical-chemical characteristics.

Mixtures with imidazole are widely used in medical practice as medicines and they have following biological activities:

- Antibacterial and antifungal activity.
- Anti-inflammatory and analgesic activity.
- Anti-TB activity.
- antidepressant activity.
- anti-tumor activity.
- anti-fever Activity.
- anti-HIV activity and more.

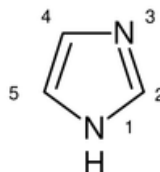
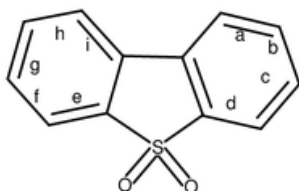
Miconazole, econazole, cetoconazole because of their low toxicity and wide anti-bacterial spectrum that covers mycelium fungus and gram-positive bacteria is used as antifungal medicine [1-5].

Thiofene and benzothiofene are very actives that are used as building materials in medical chemistry. Benzothiofene combination with other cycling systems are used as anti-allergic, pain-killer, anti-fever, eye hypertensive drug [6-9].

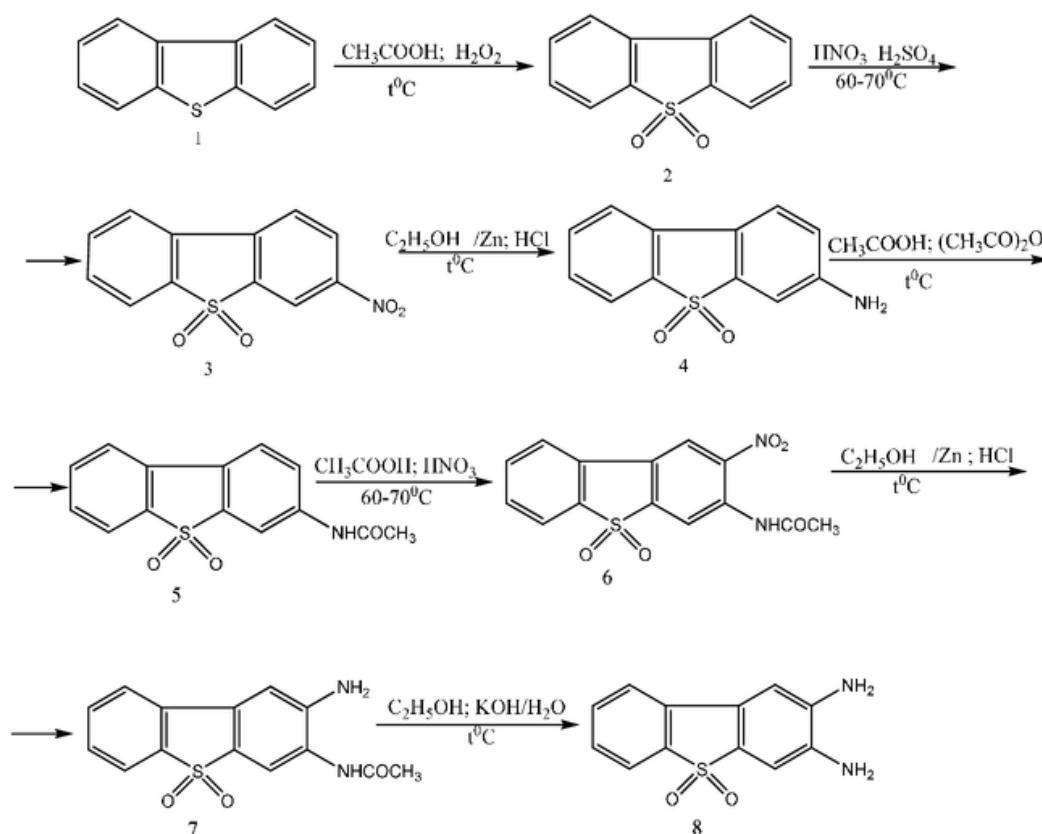
### 2. Results and Discussion

In our latest works basing of benzimidazole/benzotriazole and thiophenes tetracyclic systems were successfully integrated [10-14]. Synthesized compounds displayed high antimicrobial activity in the initial researches. In the current work, we aimed to create tetracyclic system, where imidazole nucleus would be annihilated with the tricycled system of thiophen-dioxide

Previous article covers combination biologically active molecules – imidazole and dibenzothiofene – into one molecule. Based on the present heterocycle fragments combination is expected changes in biological activeness intensity and/or directions. More than one compound in their mixtures are given as medical drugs on market.



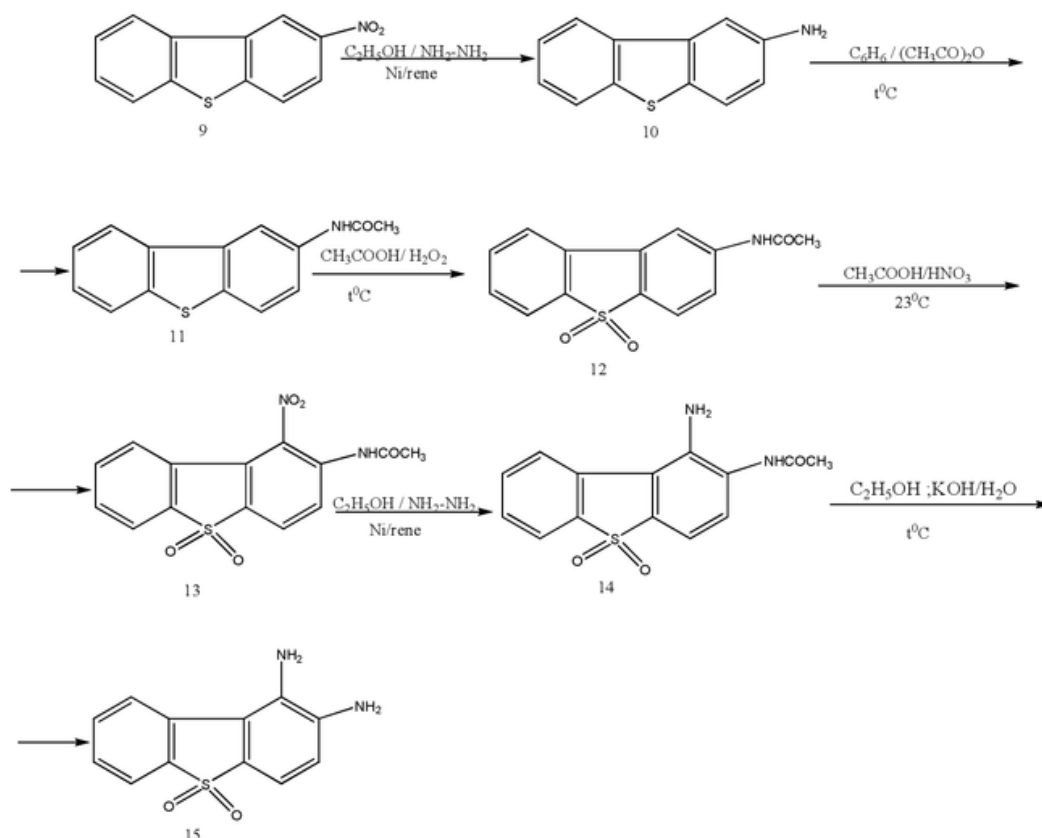
To get tetracyclic mixtures we need o-diamine compounds. Imidazole cycle annelate location depends on amino-groups configuration in diamines. Our aim is to get 1,2- and 2,3 –diamino dibenzothiofene – 5.5 – dioxide. As an initial compound in both of the cases we take dibenzothiofene (1) ( scheme 1). By oxygenation compound (1) with hydrogen peroxide we get dibenzothiofene – 5.5 dioxide (2) [11]. By nitrating compound (2) in nitric acid and sulfuric acid we get 3 – nitrodibenzothiofene – 5.5dioxide (3). By the compound (3) in restoring hydrochloric acid with zinc dust we get 3–aminodibenzothiofene (4). By compound (4) acylation with acetic anhydride in acetic acid area we get 3 – acetamino-dibenzothiofene – 5.5 dioxide (5), and with its nitration with nitrating mixture: nitric acid / sulfuric acid accepts 2- nitro, 3- acetaminodibenzothiofene – 5.5dioxide (6) whose nitrates in recovery nitrating mixture with zinc dust we get 2-amino, 3–acetaminodibenzothiofene 5.5 – dioxide (7). By hydrolyzing compound (7) we get 2,3 – diaminodibenzothiofene – 5.5 dioxide (8).



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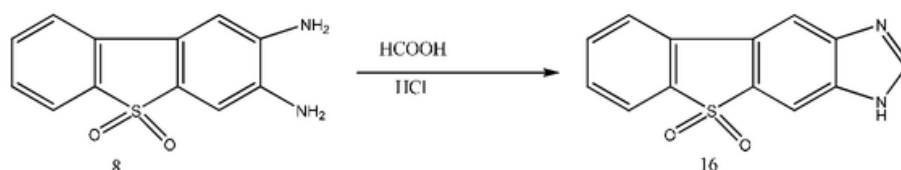
by following scheme: By dibenzothiophene (1) nitration with nitrating agent (nitric acid / sulfuric acid) we get 2 – nitrodibenzothiophene (9), by its recovery with hydrazinhydrate and nickel/rene in ethanol area we get 2 – amino-dibenzothiophene (10). By acylation of compound (9) with acidic anhydride in benzen area we get 2 – acetamino-dibenzothiophene (11), by its oxygenation with hydrogen peroxide we get 2 – acetaminodibenzothiophene – 5.5 dioxide (12). By nitration compound (11) with smoking nitric acid in acetic acid area we get 1 – nitro, 2 – acetaminodibenzothiophene – 5.5 dioxide (13). By its recovery with hydrazynhydrat and nickel/rene in ethanol area we get 1-amino, 2 – acetaminodibenzothiophene - 5.5dioxide (14). By hydrolyzing compound (14) sodium hydroxide in ethanol area we get 1.2 – diamino

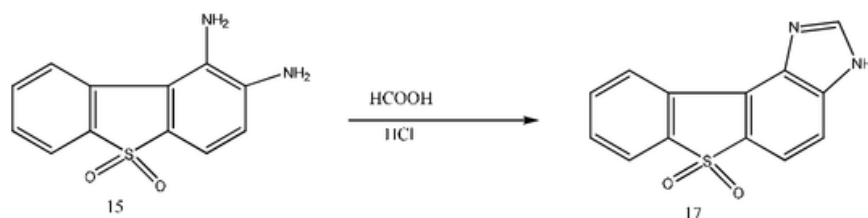


dibenzothiophene – 5.5dioxide (15) (scheme 2).

## scheme 2

Isomeric tetracyclic systems 3H-imidazole[4,5-b]di-benzothiophene-5,5dioxide and 3H-imidazole[4,5-a]dibenzothiophene-5,5dioxide (15),(16) are obtained from diamines (7),(14) by condensation with formic acid at the presence of a catalytic amount of hydrochloric acid at the modified Phillips reaction conditions (scheme3)





**scheme 3**

The originally synthesized compounds were tested by IR , <sup>1</sup>H-PMR and mass-spectroscopy methods and the chemical structure was confirmed.

### Experiment

IR spectra were recorded on spectrum meter "Thermo Nicolet" Avatar 370. <sup>1</sup>H NMR spectra were recorded on spectrometer Bruker WM-400 (400 MHz) in DMSO-d<sub>6</sub>, TMS internal standard. Elemental analysis was performed on the analyzer HP-165B CHN. Melting point is defined on the apparatus "Mel-Temp 30" control of the reaction and purity of the products was carried out on the plates

**Dibenzothiophene-5,5-dioxide (2)** – 18,4g. (0,1moles) dibenzothiophene (1) is mixed in 100ml ice Acetic acid and then heated. Aside with boiling and stirring 30ml (33%) hydrogen peroxide with drops is added. After adding hydrogen peroxide white colored crystals are precipitated. The reaction area is delayed under boiling and stirring processes for 1 hour. After adding 10ml hydrogen peroxide and boiling lasts for 30 minutes more. The compound is delayed 24 hours and filtrate, monoxide stays on filter paper, and dioxide precipitates on filter paper, that is processed with water before neutral area and is dried. It is crystallized with 96% ethanol. We receive 20,6g. dibenzothiophene-5,5-dioxide(2). M=216; C<sub>12</sub>H<sub>8</sub>O<sub>2</sub>; yield : 95,3%. T<sub>m.p.</sub>=231°C, Lit. T<sub>m.p.</sub>=232-233°C [ 15 ]. white needle -like crystals. Control - Chlorophorm : Ethyl acetate -3:1.

**3 -Nitrodibenzithiophene-5,5-dioxide(3)** – 11,4 g. (0,05 moll) dibenzothiophene 5,5dioxide is added to 40 ml concentrated sulphur acid. Drop by drop we add 34.2 ml smoking nitric acid (d=1.5). temperature remains 60-70°C degree during 20 minutes, later cold the mixture and put into icy water. Yellow precipitate in filtered, washed with water, dried and crystalized in acetone. There is 3–nitrodibenzothiophene - 5.5 dioxide (3) left on the filter. We get 13 g. 3–nitrodibenzothiophene – 5.5 dioxide (3). Yellow crystals. M = 261; C<sub>12</sub>H<sub>7</sub>NO<sub>4</sub>S; yield 94%; T<sub>mp.</sub>=264°C; liter. T<sub>mp.</sub>=265-266°C; [16] . Control: Chlorophorm- Ethilacetat 3:1

**3- Aminodibenzithiophen-5,5-dioxide ( 4)** – 12.2 g. (0.04 moll) 3-nitrodibenzothiophene – 5.5 dioxide (3) add into 481 ml 96% ethanol and add more 70 ml 31% hydrochloric acid. During boiling and puring 23.5g. zinc dust is added little by little. Yellowish reaction area becomes transparent red. Reaction takes 40-45 mins. Reaction area is filtered and water is added. It gives red precipitate which is filtered and orange filtrate is affected by 40% sodium hydroxide. Sediment is filtered again and amin from filtrate is

extracted by ethylacetat. The solvent is removed and dried at room temperature. It is crystalized in 96% ethanol. After the drying we get 9.5 g. Yellow-greenish crystals. Control: Chlorophorm. Yield – 88.7% M=231; C<sub>12</sub>H<sub>9</sub>NO<sub>2</sub>S; T<sub>mp.</sub>=256-258°C lit. T<sub>mp.</sub>=259-260°C [16].

**3 -Acetaminodibenzithiophene-5,5-dioxide (5)** 1,1 gr (0.004 moll) 3-aminodibenzo-thiophene – 5.5 – dioxide (4) is added to 68.75ml glacial acetic acid under stirring condition. The drops of 1ml acetic anhydride was added and yellow color crystals was precipitated. The mixture was kept at stirring and 25 ing conditions for 30 minutes, was hotly filtered and washed with water up neutral reaction. Then was dried at room temperature and crystalized with 11 nol. Control – ethyl acetate: Ether 3:1. Yields: 1.4g. 95.2%; T<sub>mp.</sub>=317-319°C. M=273. Anal. Calc. For. C<sub>14</sub>H<sub>11</sub>NO<sub>3</sub>S; C- 61.52; H- 4.06; N- 5.12; S- 11.73%. Found: C- 61.48; H- 4.08; N- 5.25; S- 11.72%. IR (KBr) ν<sub>max</sub> (cm<sup>-1</sup>): 3440 (NH); 3245 (CH<sub>3</sub>); 1704 (C=O); 1550(CN); 1157(SO<sub>2</sub>). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) (ppm): 2.07 (3H, s, J= 2.09, CH-3), 7.50 (1H, m, J<sub>6,5</sub>=7.73, J<sub>6,7</sub>=7.33, J<sub>8,5</sub>=0.91, J<sub>6,8</sub>=0.91, H-6), 7.56(1H, bs, NH), 7.61(1H, m, J<sub>7,5</sub>=1.11, J<sub>7,6</sub>=7.53, J<sub>7,8</sub>=7.73, J<sub>7,5</sub>=2.23, H-7), 7.71(1H, m, J<sub>5,6</sub>=7.73, J<sub>5,7</sub>=1.11, J<sub>5,8</sub>=0.63, H-5), 7.83(1H, m, J<sub>8,5</sub>=0.63, J<sub>8,6</sub>=7.50, J<sub>8,7</sub>=7.73, H-8), 8.02(1H, m, J<sub>9,3</sub>=0.91, J<sub>9,1</sub>=2.33, H-9), 8.17(1H, d, J<sub>1,3</sub>=0.91, J<sub>1,9</sub>=8.13, H-1), 8.53(1H, d, J<sub>3,1</sub>=2.33, J<sub>3,9</sub>=0.91, H-3). m/z: 273.05 (100.0%), 274.05 (16.2%), 275.04 (4.5%), 275.05 (1.9%)

**2-Nitro,3-acetaminodibenzithiophene-5,5-dioxide(6)**– 2 g. (0.007 moll) 3 – acetaminodibenzothiophene – 5.5 dioxide (5) is added to 39 ml ) glacial acetic acid and 6.3 ml nitric acid drop by drop (d=1.5) and 2 ml concentrated sulphuric acid are added. Reaction takes place on 60-70°C degree. Lemon-yellow 24 crystals are filtered and washed by water till neutral reaction, later dried. It is crystalized in 96% ethanol. Control: Chlorophorm:Ethilacetate 1:1. Yields: 1.8g. 78.3%; T<sub>mp.</sub>=292-293°C. M=318. Anal. Calc. For. C<sub>14</sub>H<sub>10</sub>N<sub>2</sub>O<sub>5</sub>S; C- 52.83; H- 3.17; N- 8.80; S- 10.07 %. Found: C- 52.80; H- 3.14; N- 8.84; S- 10.10 %. IR (KBr) ν<sub>max</sub> (cm<sup>-1</sup>): 3440 (NH); 3245 (CH<sub>3</sub>); 1700(C=O); 1535(CN); 1532 (NO<sub>2</sub>); 1140(SO<sub>2</sub>) <sup>2</sup> <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) (ppm): 2.24 (3H, s, J= 2.10, CH-3), 7.50 (1H, m, J<sub>6,5</sub>=7.73, J<sub>6,7</sub>=7.53, J<sub>6,8</sub>=1.00, H-6), 7.60(1H, m, J<sub>7,5</sub>=1.00, J<sub>7,6</sub>=7.53, J<sub>7,8</sub>=7.75, H-7), 7.70(1H, m, J<sub>5,6</sub>=7.73, J<sub>5,7</sub>=1.00, J<sub>5,8</sub>=0.63, H-5), 7.98(1H, m, J<sub>8,5</sub>=0.63, J<sub>8,6</sub>=1.00, J<sub>8,7</sub>=7.75, H-8), 8.74(1H, d, J<sub>3,9</sub>=0.71, H-3), 8.81(1H, m, J<sub>9,3</sub>=0.71, H-9), 10.31(1H, bs, NH). m/z: 318.03 (100.0%), 319.03 (16.7%), 320.03 (4.8%), 320.04 (2.1%)

**2 -Amino, 3 -Acetaminodibenzithiophene-5,5-dioxide (7)**– 1,1 gr (0.99 moll) 2-nitro-3 – acetaminodibenzothiophene-5.5 dioxide (6) is added to 75 ml 96% ethanol and 8.8ml 31% hydrochloric acid and while boiling 3.6 g. zinc dust is added too by portions. Synthesis is just like in case of mixture (4). After crystalizing in ether it gives dark yellow 5 crystals. Control: chlorophorm:ethylacetate:ether 1:3:1. Yields: 0.8g. 80%; T<sub>mp.</sub>=264-265°C. M=288. Anal. Calc. For. C<sub>14</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>S; C- 58.32; H-4.20; N- 9.72; S-11.12 %. Found: - 58.30; H-4.24; N- 9.69; S-11.10 %. IR (KBr) ν<sub>max</sub> (cm<sup>-1</sup>): 3440 (NH); 3300 (NH<sub>2</sub>); 3240 (CH<sub>3</sub>); 1700(C=O); 1530(CN); 1150(SO<sub>2</sub>). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) (ppm): 2.01 (3H, s, J= 2.09, CH-3), 4.59(2H, s, NH-2), 6.29(1H, bs, NH), 7.50 (1H, m, J<sub>6,5</sub>=7.73, J<sub>6,7</sub>=7.53, J<sub>6,8</sub>=1.00, H-6), 7.53(1H, m, J<sub>7,5</sub>=1.11, J<sub>7,6</sub>=7.53, J<sub>7,8</sub>=7.75, H-7), 7.63(1H, m, J<sub>5,6</sub>=7.73, J<sub>5,7</sub>=1.11, J<sub>5,8</sub>=0.63, H-5), 7.81(1H, m, J<sub>8,5</sub>=0.63,

$J_{8,6}=1.00$ ,  $J_{8,7}=7.75$ , H-8), 8.04(1H, d,  $J_{3,9}=0.71$ , H-3), 8.06(1H, m,  $J_{9,3}=0.71$ , H-9). m/z: 288.06 (100.0%), 289.06 (16.2%), 290.05 (4.5%), 290.06 (1.9%)

**2,3 -Diaminodibenzothiophene-5,5-dioxide(8)**–0.8 g. (0.002 mol) 2-amino,3-acetaminodibenzothiophene – 5.5 – dioxide (7) is added to 20 ml 96% ethanol and 30 ml water with 5 g. KOH. Boiling and pouring takes 30 mins. Crystals are filtered in hot condition, washed with water till neutral reaction and dried later. It gives dark yellow crystals. Control: benzol:ethylacetate 3:1. Yields: 0.46g. 78%; M=246.  $T_{m.p.}=243-246^{\circ}\text{C}$ . M 246; Anal. Calc. For.  $\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}_2\text{S}$ ; C- 58.52; H-4.09; N,- 11.37; S- 13.02 %. Found: C- 58.50; H-4.12; N,-11.33; S- 13.06 %. IR (KBr)  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ): 3400, 3300 ( $\text{NH}_2$ ); 1150( $\text{SO}_2$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ) (ppm): , 4.57(2H, s, NH-2), 7.50(1H, m,  $J_{6,5}=7.73$ ,  $J_{6,7}=7.53$ ,  $J_{6,8}=1.00$ , H-6), 7.53(1H, m,  $J_{7,5}=1.11$ ,  $J_{7,6}=7.53$ ,  $J_{7,8}=7.75$ , H-7), 7.67(1H, m,  $J_{8,5}=0.63$ ,  $J_{8,6}=1.00$ ,  $J_{8,7}=7.75$ , H-8), 7.70(1H, m,  $J_{5,6}=7.73$ ,  $J_{5,7}=1.11$ ,  $J_{5,8}=0.63$ , H-5), 7.76(1H, s,  $J_{9,3}=0.71$ , H-9). m/z: 246.05 (100.0%), 247.05 (14.0%), 248.04 (4.5%), 248.05 (1.4%)

**2- Nitro-dibenzothiophene(9) 2- Aminodibenzothiophene (10) 2- Acetaminodibenzothiophene-5,5-dioxide(11)** see [11]

**2- Acetaminodibenzothiophene-5,5-dioxide (12)** – 6 g. (0.024 mol) 2-acetamino-dibenzothiophene (11) is added to 24 ml glacial acetic acid, and while boiling and pouring is added 10 ml 33% hydrogen peroxide. Reaction goes just like in case of compound (2). After crystalizing in spirit it gives white crystals. Control: Chlorophorm:ethylacetate 3:1. Yields: 5g. 73.6%;  $T_{m.p.}=272-274^{\circ}\text{C}$ . M 273; Anal. Calc. For.  $\text{C}_{11}\text{H}_9\text{NO}_3\text{S}$ ; C- 61.52; H-4.06; N-5.12; ; S- 11.73; %. Found: C- 52.80; H-3.20; N- 8.85; S- 10.00 %. IR (KBr)  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ): 3445 ( $\text{NH}$ ); 3235 ( $\text{CH}_3$ ); 1700( $\text{C}=\text{O}$ ); 1555( $\text{CN}$ ); 1157( $\text{SO}_2$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ) (ppm): 2.09 (3H, s,  $J=2.09$ , CH-3), 6.98 (1H, d,  $J_{2,3}=8.60$ , H-2), 7.50 (1H, m,  $J_{6,5}=7.73$ ,  $J_{6,7}=7.53$ ,  $J_{6,8}=1.12$ , H-6), 7.67(1H, m,  $J_{7,5}=1.11$ ,  $J_{7,6}=7.55$ ,  $J_{7,8}=7.73$ , H-7), 7.82(1H, m,  $J_{8,5}=0.63$ ,  $J_{8,6}=1.12$ ,  $J_{8,7}=7.75$ , H-8), 7.86(1H, m,  $J_{5,6}=7.73$ ,  $J_{5,7}=1.11$ ,  $J_{5,8}=0.63$ , H-5), 7.89(1H, d,  $J_{3,2}=8.60$ ,  $J_{3,9}=0.71$ , H-3), 8.46(1H, m,  $J_{9,2}=2.13$ ,  $J_{9,3}=0.71$ , H-9), 9.87(1H, bs, NH). m/z: 273.05 (100.0%), 274.05 (16.2%), 275.04 (4.5%), 275.05 (1.9%);

**1-nitro-2acetaminodibenzothiophene-5,5-dioxide (13)**–5g.(0.018mol) 2 – acetaminodibenzo-thiophene-5.5 dioxide (12) is added to 100 ml glacial acetic acid and drop by drop is added 16 ml nitric acid ( $d=1.5$ ). Reaction takes place on  $23^{\circ}\text{C}$  degree during 40 mins. Limon-yellow crystals are affected by just like mixture (6). It is crystalized in 96% ethanol. Control: Chlorophorm:ethylacetat 1:1; Yields: 72.7%;  $T_{m.p.}=256-258^{\circ}\text{C}$ . M 318; Anal. Calc. For.  $\text{C}_{14}\text{H}_{10}\text{N}_2\text{O}_5\text{S}$ ; C- 52.83; H-, 3.17; N- 8.80; S- 10.07 %.

Found: C- 52.80; H-3.20; N- 8.85; S- 10.00 %. IR (KBr)  $\nu_{\max}$  (cm<sup>-1</sup>): 3445 (NH); 3250 (CH<sub>3</sub>); 1710 (C=O); 1540 (CN); 1530 (NO<sub>2</sub>); 1145 (SO<sub>2</sub>). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) (ppm): 2.26 (3H, s, *J*=2.09, CH-3), 7.49 (1H, m, *J*<sub>6,5</sub>=7.73, *J*<sub>6,7</sub>=7.53, *J*<sub>6,8</sub>=1.05, H-6), 7.74 (1H, d, *J*<sub>2,3</sub>=8.60, H-2), 7.80 (1H, m, *J*<sub>7,5</sub>=1.13, *J*<sub>7,6</sub>=7.53, *J*<sub>7,8</sub>=7.77, H-7), 7.83 (1H, m, *J*<sub>8,5</sub>=0.63, *J*<sub>8,6</sub>=1.05, *J*<sub>8,7</sub>=7.76, H-8), 8.01 (1H, m, *J*<sub>5,6</sub>=7.73, *J*<sub>5,7</sub>=1.13, *J*<sub>5,8</sub>=0.63, H-5), 8.22 (1H, d, *J*<sub>3,2</sub>=8.60, H-3), 10.31 (1H, bs, NH). m/z: 318.03 (100.0%), 319.03 (16.7%), 320.03 (4.8%), 320.04 (2.1%).

**1-amino-2-acetaminodibenzothiophene-5,5-dioxide(14)**-In three-neck flask with mechanical stirrer, back-freeze and dropper funnel we put 4 mg (0.012 moll) 1-nitro -2 acetaminodibenzothiophene - 5.5 dioxide (13) and 142 ml 96% ethanol in constant boiling and pouring process is added rene/Ni catalyst in small portions. Therefore drop by drop it is added 6 ml hydrazine hydrate. Reaction mass becomes transparent. Mixture is boiled two more hours, later is filtered and cold. Cold gives whitish-violate sediment crystals that are filtered and washed till neutral condition. Control: benzol:ethylacetate 3:1 it gives whitish-violate crystals. Yields: 2.7g. 75%; T<sub>m.p.</sub>=282-283°C. M 288.32; Anal. Calc. For C<sub>14</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>S; C- 58.32; H- 4.20; N- 9.72; S- 11.12%. Found: C- 58.22; H- 4.25; N- 9.70; S- 11.15%. IR (KBr)  $\nu_{\max}$  (cm<sup>-1</sup>): 3445 (NH); 3310 (NH<sub>2</sub>); 3240 (CH<sub>3</sub>); 1710 (C=O); 1530 (CN); 1155 (SO<sub>2</sub>). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) (ppm): 2.03 (3H, s, *J*=2.09, CH-3), 4.50 (2H, NH-2), 6.21 (1H, bs, NH), 6.92 (1H, d, *J*<sub>2,3</sub>=8.60, H-2), 7.02 (1H, d, *J*<sub>3,2</sub>=8.60, H-3), 7.42 (1H, m, *J*<sub>6,5</sub>=7.75, *J*<sub>6,7</sub>=7.55, *J*<sub>6,8</sub>=1.00, H-6), 7.51 (1H, m, *J*<sub>8,5</sub>=0.62, *J*<sub>8,6</sub>=1.00, *J*<sub>8,7</sub>=7.75, H-8), 7.65 (1H, m, *J*<sub>7,5</sub>=1.11, *J*<sub>7,6</sub>=7.55, *J*<sub>7,8</sub>=7.75, H-7), 7.84 (1H, m, *J*<sub>5,6</sub>=7.75, *J*<sub>5,7</sub>=1.11, *J*<sub>5,8</sub>=0.62, H-5), m/z: 288.06 (100.0%), 289.06 (16.2%), 290.05 (4.5%), 290.06 (1.9%).

**1,2-diaminodibenzothiophene -5,5-dioxide(15)** -adding 0,8g. (0.002 moll) 1-amino- 2 - acetaminodibenzothiophene -5.5 dioxide (14) into 20 ml 96% ethanol and 20 ml water with 5 g. KOH. Remain it boiling and pouring during 30 mins. Filter the crystals, wash with water till neutral reaction, dry. We get light yellow crystals. Control: Benzene:Ethilacetat 3:1. Yields: 0,46g. 74%; T<sub>m.p.</sub>=297°C. M 246.28; Anal. Calc. For C<sub>12</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub>S; C- 58.52; H- 4.09; N- 11.37; S- 13.02 %. Found: C- 58.50; H- 4.13; N- 11.34; S- 13.00 %. IR (KBr)  $\nu_{\max}$  (cm<sup>-1</sup>): 3400- 3300 (NH<sub>2</sub>); 1150 (SO<sub>2</sub>). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) (ppm): 4.53-4.56 (2H, NH<sub>2</sub>-1, NH<sub>2</sub>-2), 6.08 (1H, d, *J*<sub>2,3</sub>=8.30, H-2), 7.13 (1H, d, *J*<sub>3,2</sub>=8.30, H-3), 7.42 (1H, m, *J*<sub>6,5</sub>=7.73, *J*<sub>6,7</sub>=7.53, *J*<sub>6,8</sub>=1.00, H-6), 7.44 (1H, m, *J*<sub>8,5</sub>=0.63, *J*<sub>8,6</sub>=1.00, *J*<sub>8,7</sub>=7.75, H-8), 7.57 (1H, m, *J*<sub>7,5</sub>=1.11, *J*<sub>7,6</sub>=7.53, *J*<sub>7,8</sub>=7.75, H-7), 7.70 (1H, m, *J*<sub>5,6</sub>=7.73, *J*<sub>5,7</sub>=1.11, *J*<sub>5,8</sub>=0.63, H-5), m/z: 246.05 (100.0%), 247.05 (14.0%), 248.04 (4.5%), 248.05 (1.4%);

3H-imidazo-[4,5-b]dibenzothiophene-5,5-dioxide (16),  
imidazo-[4,5-a]-dibenzothiophene-5,5-dioxide (17).

3H-

0.2 g. (0.007 mol) diamine put into 100 ml three-neck flask and add 1 ml (0.02 mol) formic acid (HCOOH) and 1 ml 31% hydrochloric acid (HCl). Suspension is diluted while boiling and pouring. It takes about 30 mins and after add 50 ml water and alkalize with liquid ammonia until ammonia smell is given. They are filtered and washed till neutral reaction, crystalized into the ethanol. Control – Ether:hHexan:eEthilacetat = 5:1:3

**3H-imidazo-[4,5-b]-dibenzothiophene-5,5-dioxide (16)** Yields: 0.17g; 82%;  $T_{m.p.}=225-227^{\circ}\text{C}$ . White yellowish crystals. M 256.28; Anal. Calc. For.  $\text{C}_{13}\text{H}_8\text{N}_2\text{O}_2\text{S}$ ; C- 60.93; H- 3.15; N-10.93; S- 12.51%. Found: C- 60.90 H- 3.12; N-10.88; S- 12.46%. IR (KBr)  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ): 3410 (NH); 1155( $\text{SO}_2$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ) (ppm): 7.50(1H, m,  $J_{7,6}=7.73$ ,  $J_{7,8}=7.53$ ,  $J_{7,9}=1.00$  H-7), 7.63(1H, m,  $J_{8,7}=7.53$ ,  $J_{8,9}=7.75$ ,  $J_{8,6}=1.11$ , H-8), 7.80 (1H, m,  $J_{6,9}=0.63$ ,  $J_{6,7}=7.73$ ,  $J_{6,8}=1.11$ , H-6), 7.88 (1H, m,  $J_{9,8}=7.75$ ,  $J_{9,7}=1.00$ ,  $J_{9,6}=0.63$ , H-9), 7.99 (1H, d,  $J_{10,4}=7.75$ , H-10), 8.42(1H, d,  $J_{4,10}=0.91$ , H-4), 8.53 (1H, d, H-2), 7.70(1H, m,  $J_{5,6}=7.73$ ,  $J_{5,7}=1.11$ ,  $J_{5,8}=0.63$ , H-5), 10.20(1H, bs, NH). m/z: 256.03 (100.0%), 257.03 (15.7%), 258.03 (5.2%);

**3H-imidazo-[4,5-a]-dibenzothiophene-5,5-dioxide(17)** Yields: 0.16g. 77%;  $T_{m.p.}=337^{\circ}\text{C}$ . Dark yellow crystals. M 256.28; Anal. Calc. For.  $\text{C}_{13}\text{H}_8\text{N}_2\text{O}_2\text{S}$ ; C- 60.93; H- 3.15; N-10.93; S- 12.51%. Found: C- 60.94 H- 3.13; N-10.90; S- 12.48%. IR (KBr)  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ): 3400 (NH); 1150( $\text{SO}_2$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ) (ppm): 7.55(1H, m,  $J_{8,7}=7.73$ ,  $J_{8,9}=7.53$ ,  $J_{8,6}=1.00$ , H-8), 7.85 (1H, m,  $J_{9,8}=7.53$ ,  $J_{9,7}=1.11$ ,  $J_{9,10}=7.75$ , H-9), 7.89(1H, d,  $J_{4,5}=8.60$ , H-4), 7.91(1H, d,  $J_{5,4}=8.60$ , H-5), 8.04(1H, m,  $J_{7,10}=0.63$ ,  $J_{7,8}=7.73$ ,  $J_{7,9}=1.11$ , H-7), 8.14 (1H, m,  $J_{10,9}=7.75$ ,  $J_{10,8}=1.00$ ,  $J_{10,7}=0.63$ , H-10), 8.45 (1H, d, H-2), 10.20(1H, bs, NH). m/z: 256.03 (100.0%), 257.03 (15.7%), 258.03 (5.2%).

## Conclusion

As a result of successive transformations of dibenzothiophene we get 1.2 and 2.3 diaminodibenzothiophene 5.5 dioxides where from by Phillips reaction we get 3H – imidazole [4,5-b]dibenzothiophene-5.5dioxide and 3H-imidazole [4,5-a] dibenzothiophene 5.5- dioxide. These compounds represent foundation cycles and on their bases it is possible to get various derivatives with expected biological activeness.

## References:

1. [Subramaniyan Arulmurugan](#), [Helen P. Kavitha](#), [Samiyappan Sathishkumar](#) and [Rajaram Arulmozhi](#), Biologically Active Benzimidazole Derivatives, *Mini-Reviews in Organic Chemistry*, 12(2): 178-195.
2. [Kaushik Chanda](#), [Sreerama Rajasekhar](#), [Barnali Maiti](#) and [Balamurali MM](#), Synthesis and Medicinal Applications of Benzimidazoles: An Overview, *Current Organic Synthesis*, Volume 13 (E-pub ahead of print) Volume 13, 6 Issues, 2016]
3. [\[S. Khabnadideh, Z. Rezaei, A. Khalafi-Nezhad, K. Pakshir, A. Roosta and Z Baratzadeh](#), Design and Synthesis of Imidazole and Benzimidazole Derivatives as Antifungal Agents, *Anti-Infective Agents*, 7(3):215-218.2009]
4. [\[Emre e Montes, Fatih Yilmaz, Fatih Saban Beri s, Olcay Bekircan and Bahittin Kahveci](#).Microwave-Assisted Synthesis of Some New Benzimidazole Derivatives with their Antimicrobial Activity, *Current Microwave Chemistry*, 2(1): 32-39.2015]
5. [\[Leyla Yurttas, Yusuf Ozkay, Hulya Karaca, Yagmur Tunali and Zafer Asim Kaplancikli](#), Synthesis and Antimicrobial Evaluation of Some 2,5-Disubstituted Benzimidazole Derivatives,*Letters in Drug Design & Discovery*, 10(6): 486-491. 2013];
6. M. Avkiran, M. S. Marber, Na(+)/H(+) exchange inhibitors for cardioprotective therapy: progress, problems and prospects.J. Am. Coll. Cardiol. 2002, 39, 747.
7. M. Karmazyn, X. T. Gan, R. A. Humphreys, H. Yoshida, K. Kusumoto, Circ. The Myocardial Na1-H1 Exchange Structure, Regulation, and Its Role in Heart isease Res. 1999, 85, 777.
8. A. J. Bridges, A. Lee, E. C. Maduakor, C. E. Schwartz, The synthesis of three 4-substitutedbenzo[b]thiophene-2-carboxamidines as potent and selective inhibitors of urokinase; Tetrahedron Lett. 1992, 33, 7499.
9. S. Lee, H. Lee, K. Yang Yi, B. Ho Lee, S. Yoo, K. Leec N. Sook; Chob4-Substituted (benzo[b]thiophene-2-carbonyl)guanidines as novel Na+/H+ exchanger isoform-1 (NHE-1) inhibitors. Bioorganic & Medicinal Chemistry Letters 15 (2005) 2998–3001.
10. M.Maisuradze, G. Ugulava, N. Bolkvadze, G. Phalavandishvili, N. Gaxokidze, M.Matnadze. Some New Derivatives of3H-Benzo (b)Furobenzotriazole. Journal of Chemistry and Chemical Engineering. USA Vol.7, No. 7, 621-625 2013
11. 7.M.Maisuradze,TKhoshtaria, N. Gaxokidze, L.Kurkovskaia. [Synthesis of benzo\[b\]thienof\[3,2-e\]benzimidazoles, first representatives of a new heterocyclic system](#). *Chemistry of Heterocyclic Compounds*. Vol. 44,(8), pp 1024-1026, 2008;
12. 8.M.Maisuradze, G.Ugulava. *The Triazole and Thiophene Containing New Heterocyclic Systems*. Journal of Chemistry and Chemical Engineering. USA. Vol.6, No. 4, p 378-383 2012;
13. 9.M.G.Maisuradze, V. O. Ananiashvili, N. Z. Gaxokidze,M. M. Matnadze Some novel derivatives of 3H-benzo[b]thiophen[3,2-e]benzimidazole. *Chemistry of Heterocyclic Com- pounds*. Vol. 48, No. 12, p.1801-1804, 2013;

14. 10.M.G.Maisuradze, V. O. Ananiashvili, N. Z. Gaxokidze, M. M. Matnadze, S. P. Tsqvitaia. Synthesis of novel heterocyclic systems, benzo[b]furobenzimidazoles. *Chemistry of Heterocyclic Compounds*, Vol. 48, No. 7, p 1125-1126, 2012;
15. H. Gilman, D.L. Esway. The Oxidation of DibenzoThiofene and Phenoxathiin with Hydrogen Peroxide. *J. Am/ Chem. Soc.* v 74, N14, p 2021-2025. 1952
16. H. Gillman, A.L. Jacoby, H.A. Pacevitte. Realative reactivities og organometallic compouns. seleqtive metalations of dibenzothiophene. *J.Org. Chemistry*. V.3. N1. p.p. 120-124. 1938.

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% **1**

- 
- 7 Atkinson, Paul, Karen S. Findlay, Filip Kielar, Robert Pal, David Parker, Robert A. Poole, Horst Puschmann, Siobhan L. Richardson, Philip A. Stenson, Amber L. Thompson, and Junhau Yu. "Azaxanthonenes and azathioxanthonenes are effective sensitizers for europium and terbium luminescence", Organic & Biomolecular Chemistry, 2006.

Publication

- 
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- 
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- 
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- 
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12

[www.gccpo.org](http://www.gccpo.org)

Internet Source

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<% 1

of influenza virus hemagglutinin mediated fusion", Phosphorus Sulfur and Silicon and the Related Elements, 2014.

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[www.scialert.net](http://www.scialert.net)

Internet Source

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19

[www.patents.com](http://www.patents.com)

Internet Source

<% 1

20

Srivastava, Prakash C. Bajpai, Sangeeta .  
"Synthesis and characterization of  
bis(ferrocenylcarboxylato)telluranes.",  
Canadian Journal of Chemistry, July-August  
2007 Issue

Publication

<% 1

21

Kerry, Mark A., Gary W. Boyd, Simon P.  
Mackay, Otto Meth-Cohn, and Louise Platt.  
"The synthesis of benzo[h]quinolines as  
topoisomerase inhibitors", Journal of the  
Chemical Society Perkin Transactions 1, 1999.

Publication

<% 1

22

Ünlü, Serdar, Erden Banoglu, Shigeru Ito,  
Tokihito Niiya, Gökçen Eren, Berna Ökçelik,  
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towards cyclooxygenase inhibition", Journal of

<% 1

# Enzyme Inhibition and Medicinal Chemistry, 2007.

Publication

23

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Publication

<% 1

24

Maisuradze, Mamuka; Gaxokidze, Nana and Tsqvitaia, Sofio. "Some New Derivatives of 3*H*-benzo[*b*]Furo[3,2-*f*] Benzimidazole with Expected Biological Activity", Journal of Chemistry & Chemical Engineering, 2012.

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