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# STUDY OF REACTION OF ARYLSULFOCHLORIDES WITH BICYCLIC AMINES


***Abstract***: *The reaction of arylsulfochlorides with 6-(adamantyl-1)-2-z-3-(4-arylsulfonyl)-[2, 3-b] pyridineselenophen- or thiophen was studied. It was found that regardless of the nature of functional groups in 2-position the output of heterosulfamides with selenophens is lower than with thiophen fragment. The effort to obtain sulfamides with bicyclic amines containing nitrile group in 2-position, failed. Some adamantyl-pyridine-selenophens and – thiophens were tested as a bactericide against staphylococcus and typhoid fever. It was found that selenium containing products are more effective than sulfur-containing compounds.*



***Key words***: *heterosulfamides, aminoheterocycles, bicyclic amines, polarophil, heterocyclization, bactericide*

***Language***: *English*

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## INTRODUCTION

Medications improving brain blood circulation-nimodipine, nifedimin-(blockers of calcium channels) were produced on the basis of pyridinethion compounds. At present active searches of non-glycoside and nonadrenergic cardiotonic agents with large therapeutic are conducted. Their synthetic analogs - acrinon, proximone, milrinone are widely applied in intensive therapy. Besides, sulphamides containing pyrimidine fragments have cytostatic action that allows using them as antiviral and antineoplastic medicines. They are potential bactericides. Their antimicrobial activity and influence on various microorganisms depends by

nature of heterocycle and functional groups. Therefore, the synthesis of new sulphamides containing bicyclic compounds, by reaction of arylsulfochlorides with heterocyclic amines is urgent.

The influence of the composition of heterocycle and position of amino groups was studied. So, the location of amino groups in isoxazole strongly influences on its reactivity. During the reaction of sulfochlorides with 5-amino 3,4 dimethyl isoxazole [1] and biphenylisoxazole [2] we obtained hetarylsulfamides with high yield. Reaction of sulfochlorides with five-membered aminoheterocycles, such as oxazoles [3], pyrazole proceeds with high yields. However, the reaction of sulfochlorides with benzoxazole requires long boiling in solution of pyridine [4].

Reaction of arylsulfochlorides with piperazines, attached to them through oxygen or N-pyridylil- or pyrimidinediyle fragment, proceeds very easily. Action of radicals and functional groups on reaction wasn't observed [5]. Obtained sulphamides can be applied at diseases of CNS and decreased kidney function.

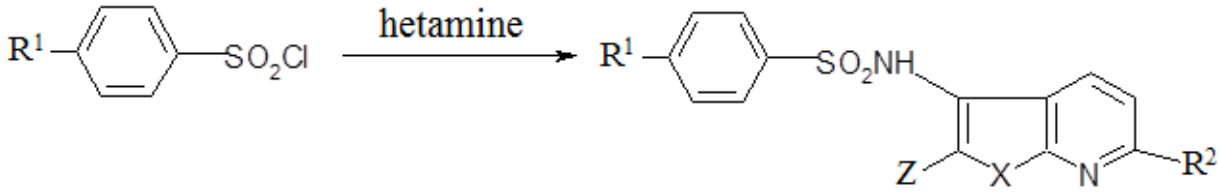
Despite contents of cinchine acid in 4-aminobenzenesulfochloride fragment, the reaction with a 2-amino-4,6-dimethylpyrimidine proceeds very easily forming sulphamides with having anti-inflammatory and analgesic activity [6].

It is found what acetamidobenzenesulfochloride in the presence of DMSO easily joins derivatives of chitosan [7]. These sulphamides have antifungal activity in ratio with Alternaria Solani and Phomopsis asparage. Pyridazinesulfonamide derivatives obtained by the reaction of sulfochlorides also have antimicrobial activity [8].

Thus, reactivity of aminoheterocycles depends on structure, existence and location of functional groups. Researches of reaction of arylsulfochlorides with adamantyl-, sulfur- and selenium containing bicyclic amines is of great interest for obtaininf of new sulfamide compounds, from the other hand for study of their bactericidal and other properties.

Adamantyl-, sulfur - and selenium containing bicyclic amines were synthesized in laboratory of chemistry of heterofunctional compounds of N.D.Zelinsky Institute of organic chemistry of RAS and were reflected in the works of prof. V.P.Litvinov [9-10].

It is found that reaction of arylsulfochloride with heterocyclic amines occurs when using freshly distilled pyridine as a solvent with a separation of chlorine hydride:




$R^1$=H, $R^2$=$Ad_1$: Z=$COOC_2H_5$, X=S (I);
Z=$COOC_6H_5$, X=Se(II); Z=COOH, X=Se(III);
Z=$COC_6H_5$, X=S (IV);
$R^1$=$CH_3$, $R^2$=$Ad_1$, Z=$COOC_2H_5$, X=S(V);
$R^1$=$CH_3$, $R^2$=$Ad_1$, Z=$CONH_2$, X=Se(VI);
$R^1$=$CH_3$, $R^2$=$CH_3$, Z=$COOC_2H_5$, X=S(VII);
$R^1$=H, $R^2$=$CH_3$, Z=$COOC_2H_5$, X=S(VIII)

It is found that in the presence of selenium atom, regardless of functional groups in 2-position, the yields of hetarylsulfamide are lower, than in sulfur atom. Besides, it should be noted that the content of such voluminous fragment like adamantyl-1 influences on yields of compounds.

Selective testing of some hetarylsulfamides (II, IV, V, VI, VII) as bactericides against staphylococcus and typhoid fever agents (S.typhi) was conducted. Obtained data are provided in table 1. As table 1 shows hetarylsulfamides containing selenium (compounds II, VI), regardless of the nature of functional groups ($COC_6H_5$, $CONH_2$) are more effective, than sulfur-containing sulphamides. They even in concentration of 0,01% in solution of 45% of ethanol within 60 min. completely destroy microorganisms of staphylococcus and stop the development of S.typhi. In comparison with compound II, sulfur-containing compound IV affects only in concentration in 0,05% for 30 min. The same is observed with compounds V and VII. Full elimination of staphylococcus happens in concentration of 0,1% for 60 min., and for S.typhi the elimination occurs in concentration of 0,05% for 30 min. In absence of adamantine fragment (compound VII) in heterocycle bactericidal action weakens.

Long latent period can be explained with large size of hetarylsulfamides and the reason of difficult penetration through membrane of microorganism.

**Table 1**

| Strains of cultures | Concentration, % | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 0,01% | | | | 0,05% | | | |
| | 20 | 30 | 40 | 60 | 20 | 30 | 40 | 60 |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| | 45% of alcohol solution in water | | | | | | | |
| staphylococcus | + | + | + | + | | | | |
| s. typhi | + | + | + | + | | | | |
| | Compound II | | | | | | | |
| staphylococcus | + | x | x | - | - | - | - | - |
| s. typhi | + | + | + | x | x | - | - | - |
| | Compound IV | | | | | | | |
| staphylococcus | + | + | + | x | x | - | - | - |
| s. typhi | + | + | + | + | + | x | - | - |
| | Compound V | | | | | | | |
| staphylococcus | + | + | + | x | - | - | - | - |
| s. typhi | + | + | + | + | x | x | - | - |
| | Compound VI | | | | | | | |
| staphylococcus | + | + | x | - | - | - | - | - |
| s. typhi | + | + | + | x | x | - | - | - |

## EXPERIMENTAL PART

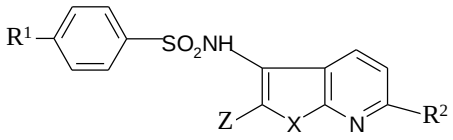
PMR-spectra of some synthesized compounds were registered on a sepctrophotometer "Bruker" with operating frequency 90 MHz, IR spectra were registered on "Nicolet-is-10".

**The synthesis of 6-(adamantyl-1) - 2-Z-3-3 (4-arylsulfonyl) - pyridine [2,3b] selenophen or – thiophen.**

General technique. 10 mmol of the appropriate heterocyclic amine was dissolved in 20-25 ml of freshly distilled pyridine and 11 mmol of arylsulfochloride was slowly added to solution. The mixture was heated in case of 50-60˚C 5-6 hours, cooled and diluted with water before drop-out of crystals, filtered, washed out 3-4 times with water, dried and recrystallized from ethanol. Physical and chemical characteristics are provided in table 2.

PMR-and IR - spectral data are given in table 3, which confirm the supposed structures.

**Table 2**




**Physical and chemical characteristics of hetarylsulfamides:**

| | Z | $R^1$ | $R^2$ | X | Yield, % | Tmelt. $^0$C | Chemical formula | Analysis, % | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | C | H | N | S |
| | | | | | | | | Found<br>Calculated, % | | | |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| I | $COOC_2H_5$ | H | $Ad_1$ | S | 96,3 | 239-240.5 | $C_{26}H_{27}N_2O_4S_2$ | 63.29<br>63.01 | 5.71<br>5.49 | 5.39<br>5.65 | 12.68<br>12.90 |
| II | $COC_6H_5$ | H | $Ad_1$ | Se | 74,9 | 178-179 | $C_{30}H_{27}N_2O_3SSe$ | 62.98<br>62.71 | 4.89<br>4.74 | 4.65<br>4.87 | --- |
| III | COOH | H | $Ad_1$ | Se | 68,6 | 179.5-181.5 | $C_{24}H_{23}N_2O_4SSe$ | 55.29<br>56.03 | 4.68<br>4.51 | 5.37<br>5.45 | --- |
| IV | $COC_6H_5$ | H | $Ad_1$ | S | 85,2 | 170-171.5 | $C_{30}H_{27}N_2O_3S_2$ | 68.02<br>68.29 | 5.40<br>5.16 | 5.11<br>5.31 | 11.96<br>12.12 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| V | $COOC_2H_5$ | $CH_3$ | $Ad_1$ | S | 91,6 | 167-168 | $C_{27}H_{29}N_2O_4S_2$ | 63.81<br>63.63 | 5.92<br>5.74 | 5.38<br>5.50 | 12.36<br>12.5 |
| VI | $CONH_2$ | $CH_3$ | $Ad_1$ | Se | 77,8 | 308-309.5 | $C_{25}H_{26}N_3O_3$ SSe | 57.29<br>56.92 | 5.19<br>4.97 | 7.76<br>7.97 | --- |
| VII | $COOC_2H_5$ | $CH_3$ | $CH_3$ | S | --- | 168-169 | $C_{18}H_{18}N_2O_4S_2$ | 56.11<br>55.37 | 4.36<br>4.65 | 7.41<br>7.17 | 16.29<br>16.4 |
| VIII | $COOC_2H_5$ | H | $CH_3$ | S | --- | 178-179 | $C_{17}H_{16}N_2O_4S_2$ | 54.61<br>54.24 | 4.44<br>4.28 | 7.09<br>7.44 | 16.88<br>17.05 |

**Table 3**

**Data of PMR- and IR-spectra.**

| № | PMR-spectra, δ, m.g. | | | | | | IR-spectra, ν, $cm^{-1}$ | | |
|---|---|---|---|---|---|---|---|---|---|
| Compound | $CH_3$ | $CH_2$ | NH или$NH_2$ | $Ad_1$ | Arom. | Pyridyl | NH | $SO_2$ | C=O |
| I | 1.95 | 2.05 Acetone-$D_6$ | 5.6 Acetone-$D_6$ | 2.55 | 7.35-7.75 | 7.65 | 3400 | 1455<br>1130 | --- |
| II | 1.30<br>1.80 | 2.05 Acetone-$D_6$ | 6.85 Acetone-$D_6$ | 2.10 | 7.4-7.45 | 7.65 | 3440 | 1450<br>1160 | 1695 |
| III | --- | 8.2 DMSO-$D_6$ | | | | | 3395 | 1455<br>1170 | 1695 |
| IV | --- | --- | --- | --- | --- | --- | 3310 | 1455<br>1165 | 1685 |
| V | 1.45 | DMSO | 7,0 $CONH_2$; 8,25 | 2,50 | 7,3-7,6 | 7,7 | 3400 $CONH_2$; 3320 | 1450<br>1145 | 1650 |
| VI | --- | --- | --- | --- | --- | --- | 3430 | 1490<br>1160 | 1720 |

**References:**


1. Chang Ming P, Ruju BC (2003) Patent USA 6541492, application. 27.12.2003. Published. 01.04.2003
2. Polniazek RO, Wang X, Debal tetreys, Pandit CR (2003) Patent USA 6515130, application. 24.08.1998. Published 04.02.2003
3. Tarisuka K, Okasi M, Yamomoto N, Misibisu Seysi K (2008) application 63-44534(Japan), application. 11.08.2006. K-Ni 61-189020. Published 23.02.2008
4. Tosheva M, Antonova A (2005) Sofia University, chemistry department. 2005, 91, p.149-152,
5. Braje WM, Haupt A, Labirch W, Grandel R, Darye R, Turner S (2008) Patent USA 7320979, application 13.04.2004. Published 22.01.2008
6. Novikov MV, Mikhailov AM, Konishim ME, Vasilyuk MV, Kotegov VP, Vakhrin MI (2009) Patent Russia. 2364594. application 09.01.2008. Published 20.08.2009
7. Zhong Zhimli, Chen Rong, Xing Ronga, Chen Xiaolin, Lui Song, Guo Zhanyong Zi Xia, Wang Lin, Li Pengcheng (2007) karbohydr Res., 2007, 342, №16. p.2390-2395
8. Mohammed MJ (2007) Bulg. Chem. Commun, 2007, 39, №2. p.152-158. РЖХ.08.23-19О.109
9. Litvinov VP, Apenova EE, Sharanin YA, Shestopalov AM (1985) Synthesis of 6-(1-adamantyl)-3-cyanopyridine1H)-one and selenone. Journal of Orgn. Chem. 1985. -21, № 3, p. 669-670.
10. Litvinov VP, Apenova EE, Sharanin YA, Shestopalov AM (1984) Synthesis of 6-(adamantyl-1)-3-cyano-2(1H)-pyridintion. Russian Chemical Bulletin. Division of Chemical Sciences-1984. №10, p. 2408.