Abstract – N-Aryl substituted 1,3,5-dithiazinan-1-yl have been synthesized (20–60 °C) in 32–95% yield by cyclocondensation of o-, p-aminobenzoic, 4-, 5-aminosalicylic acids, p-aminobenzoic acid ethyl or (β-diethylamino)ethyl esters and p-aniline sulfamide with CH₂O and H₂S (1:3:2 ratio). At ambient temperature p-aminobenzoic acid, 5-aminosalicylic acid and p-aminobenzoic acid ethyl ester together with 1,3,5-dithiazinan-1-yl substituted 1,3-thiazetidines. Cyclothiomiethylation of p-aminobenzoic acid ethyl ester (0 °C) results in N,N-diaryl-1,3,5-thiadiazinan-1-yl. Heterocyclization of p-aniline sulfamide with CH₂O and H₂S at a molar ratio of 1:6:4 (pH 1.3–1.5) was found to afford bis-1,3,5-dithiazinan-1-yl involving two amino groups. Condensation of p-aniline sulfacetamide with 37% formalin (CH₂O) and H₂S (pH 2.5) led to the compound, which was built as macroheterocycle from two fragments of p-aniline sulfacetamide molecule bound to each other by sym-dimethyl sulfide chain (CH₂SCH₂).

INTRODUCTION

In organic chemistry there is an original method for the synthesis of 1,3,5-dithiazinan-1-yl based on Wohl reaction namely multimolecular cyclocondensation of methyl amine, 37% formalin (CH₂O) and H₂S. Compounds, which contain dithiazinan ring, are used as insecticides and fungicides as well as...
additives modified and intensified product taste,\textsuperscript{2c-g} inhibitors, ferments,\textsuperscript{2h} complexons,\textsuperscript{3a-g} sorbents for gold and silver.\textsuperscript{4a,b}

For the last 5 years we systematically investigated the Wohl reaction using cyclothiomethylation of aliphatic\textsuperscript{5a} and aromatic\textsuperscript{5b} amines, amino acids,\textsuperscript{5c} aminoalcohols\textsuperscript{5d} aminophenols\textsuperscript{5e} as an example to obtain the corresponding $N$-substituted 1,3,5-dithiazinanes,\textsuperscript{5a-e} 1,3-thiazetidines\textsuperscript{5a,b,c} and 1,3,5-thiadiazinanes.\textsuperscript{5b} The direction of the cyclothiomethylation reaction depends on the structure of initial amines and reaction conditions (ratio and order of reagent mixing,\textsuperscript{5a,c} temperature,\textsuperscript{5a-e} medium $p$H), under which cyclocondensation is conducted. Thus, it was shown that in the cyclothiomethylation reaction of aliphatic\textsuperscript{5a} and aromatic\textsuperscript{5b} amines with CH$_2$O and H$_2$S (amine:CH$_2$O:H$_2$S = 1:3:2) the decrease in basicity of amines causes the increase in the yield of target 1,3,5-dithiazinan ines. Further more thorough and deep analysis of cyclocondensation of functionally-substituted anilines, namely $o$-, $m$- and $p$-aminophenols, with CH$_2$O and H$_2$S has shown, that the direction of the cyclothiomethylation reaction of aminophenols depends on the position of functional amino group.\textsuperscript{5e} Aminophenols, $o$- and $p$-isomers, were established to interact with CH$_2$O and H$_2$S as a reactant mixture (3:2 ratio) to form 1,3,5-dithiazinanines. $m$-Aminophenol under analogous conditions undergoes intermolecular condensation with CH$_2$O and H$_2$S simultaneously involving OH and NH$_2$ groups to form macroheterocycle, which contains the fragments of $m$-aminophenol molecules. Different reactivity of isomeric aminophenols under interaction with CH$_2$O and H$_2$S is caused by a change of NH$_2$ group basicity and OH group acidity according to their arrangement in aromatic ring.

Herein we report on the results of our further investigations in the field of cyclothiomethylation of functionally substituted aromatic amines in order to develop novel procedures for a synthesis of new $N$-aryl substituted 1,3,5-dithiazinanines, 1,3,5-thiadiazinanines and macroheterocycles.

**RESULTS AND DISCUSSION**

**CYCLOTHIOMETHYLATION OF AROMATIC AMINO ACIDS AND $p$-AMINOBENZOIC ACID ESTERS**

In cyclocondensation with CH$_2$O and H$_2$S there have been involved aromatic amino acids and their derivatives namely $o$- (1a) and $p$-aminobenzoic 1b acids, 4-(1c) and 5-aminosalicylic 1d acids, and also $p$-aminobenzoic acid ethyl 1e and ($\beta$-diethylamino)ethyl 1f esters. Using $o$- (1a), $p$-aminobenzoic 1b and 4- (1c), 5-aminosalicylic 1b acids as an example we have studied the influence of COOH group position in aromatic ring on the activity of NH$_2$ and OH groups in the cyclothiomethylation reaction.

Thus, condensation of aminobenzoic acid 1a with CH$_2$O and H$_2$S (1:3:2 ratio) at 20 $^\circ$C led exclusively to $o$-(1,3,5-dithiazinan-5-yl)benzoic acid 2a in 61% yield, whereas $p$-aminobenzoic acid 1b gave a mixture of $p$-(1,3,5-dithiazinan-5-yl)- (2b) and $p$-(1,3-thiazetidin-3-yl)benzoic (3b) acids with good yields (51 and
34%, respectively) (Scheme 1). Dithiazinane 2b has been selectively obtained at 60 °C in 95% yield.

\[
\begin{align*}
&1 \text{(a-d)} \quad \text{CH}_2\text{O}-\text{H}_2\text{S} / 3:2 \quad \text{2 (a-d)} + \text{3 (b,d)} \\
&2 \text{-NH}_2, R^1 = \text{H (a)}, 4 \text{-NH}_2, R^1 = \text{H (b)}, 4 \text{-NH}_2, R^1 = 2\text{-OH (c)}, 5 \text{-NH}_2, R^1 = 2\text{-OH (d)}
\end{align*}
\]

Scheme 1 Cyclothiomethylation of o- and p-aminobenzoic acids, 4- and 5-aminosalicylic acids

4-Aminosalicylic acid 1c, similar to acid 1a, reacts with CH\textsubscript{2}O and H\textsubscript{2}S to form exclusively 4-(1,3,5-dithiazinan-5-yl)-2-hydroxybenzoic acid 2c in 89% yield, and 5-aminosalicylic acid 1d, similar to acid 1b, gave a mixture of 5-(1,3,5-dithiazinan-5-yl)-2-hydrobenzoic acid 2d and 5-(1,3-thiazetidin-3-yl)-2-hydroxybenzoic acid 3d in the yields of 32 and 22%, respectively.

4-Aminosalicylic acid 1c, in which OH and NH\textsubscript{2} groups occupy meta- position, in contrast to m-aminophenol, reacts with CH\textsubscript{2}O and H\textsubscript{2}S exclusively at the amino group, probably, as a result of the intramolecular hydrogen bonding between OH and COOH groups (OH... O the ortho-effect). As is evident, the direction of cyclothiomethylation of isomeric aromatic amino acids with the aid of CH\textsubscript{2}O and H\textsubscript{2}S depends on the arrangement of functional groups in aromatic ring and their mutual influence.

Individual compounds 2a-d and 3b,d have been isolated by means of fractional crystallization. The structures of dithiazinanes 2a-d and thiazetidines 3b,d are proven by spectral methods: \textsuperscript{1}H NMR and \textsuperscript{13}C NMR, GC/MS, and also by the data of element analysis. Molecular weight was determined by Rast cryoscopic method. Heterocycle 2a was obtained earlier\textsuperscript{4a} with 81% yield by cyclocondensation of 1a with NaHS and CH\textsubscript{2}O, for which any spectral characteristics were absent.

Thus, aromatic amino acids were condensed with CH\textsubscript{2}O and H\textsubscript{2}S only at NH\textsubscript{2} group with the formation of N,S-containing heterocycles (1,3,5-dithiazinan-5-yl)-2-hydroxybenzoic acid 2c and 5-(1,3-thiazetidin-3-yl)-2-hydroxybenzoic acid 3d. The greatest yield of target dithiazinanes 2a-d was reached in temperature range from 20 to 60 °C. An increase in reaction temperature up to 80 °C led to a decrease in selectivity with formation of by-product of the reaction – 1,2,4-trithiolane.\textsuperscript{8}

By the reaction of p-aminobenzoic acid ethyl 1e or (β-diethylamino)ethyl 1f esters with CH\textsubscript{2}O and H\textsubscript{2}S (1:3:2 ratio) at 20 °C the compounds of dithiazinane row 2e,f has been obtained. Amino ester 1e in this reaction together with ethyl-4-(1,3,5-dithiazinan-5-yl) benzoate 2e gave ethyl-4-(1,3-thiazetidin-3-yl) benzoate 3e and 3,5-di(4-ethylcarboxyphenyl)-1,3,5-thiadiazinane 4e in 56, 18% and 15% yields, respectively (Scheme 2). At 60 and 80 °C the reaction resulted in a mixture of products 2e-4e. The latter compounds were isolated by column chromatography.
The regioselective synthesis of thiadiazinane 4e was carried out at 0 °C by cyclocondensation of p-aminobenzoic acid ethyl ester 1e with CH₂O and H₂S (2:3:1 ratio) in 93% yield. Heterocyclic 4e in the presence of three-molar excess of a thiomethylation mixture CH₂O-H₂S at ambient temperature was completely converted into the appropriate dithiazinane 2e.

Scheme 2. Cyclothiomethylation of p-amino benzoic acid ethyl and (β-diethylamino)ethyl esters

According to X-ray diffraction analysis the molecule of 4e has local plane of symmetry passing through C(2) and S(1) atoms (Figure 2a). The thiadiazinane ring has a chair conformation with axial cis position of (4-ethoxycarbonyl)phenylic substituent at the nitrogen atoms. In this orientation the lone pairs at the nitrogen atoms occupy cis equatorial position and are antiperiplanar to the lone pairs of the sulfur atom (conformer B).

The orbital repulsion of lone electron-pairs of the nitrogen and sulfur atoms stabilizes an axial cis position of (4-ethoxycarbonyl)phenylic substituent (anomeric effect).

Figure. General view (a) and fragment of crystal packing (b) of compound 4e in the crystal

In crystal structure above there are two types of intermolecular hydrogenous bonds (Figure 2b). The sulfur atom of one thiadiazinane molecule forms hydrogenous bonds with protons on the two aromatic
rings at C(4) and with methylene protons of another thiadiazinane molecule at C(2): HC(4)...S(1)...HC(4') и HC(2)...S(1) (where H. S distances are equal to 2.83Å (x 2) and 2.78Å, respectively). At the same time, the ester carbonyl groups of the first thiadiazinane molecule are connected with methylene protons of two other thiadiazinane molecules: O(1)...HC(1A) and O(1')...HC(1B) (distances O.. H 2.54Å (x 2)).

In the ¹H NMR spectra of dithiazinane cycles 2a-f one could observe two singlets of methylene protons at δH 3.40-4.22 (SCH₂S) and 4.15-5.20 ppm (NCH₂S) with integrated intensities ratio of 1:2. The ¹³C NMR spectra contain signals at δC 30.61-34.80 (SCH₂S) and 44.51-56.89 ppm (NCH₂S) belonging to the carbon atoms. The ¹H NMR spectrum of thiazetidine cycle (compounds 3b,d,e) exhibits singlets of methylene protons (NCH₂S) at δH 4.30-5.15 ppm, while the ¹³C NMR spectra contain peaks at δC 51.97-54.60 ppm. In the ¹H NMR spectra of thiadiazinane 4e the signals for CH₂SCH₂ and NCH₂S methylene protons are observed at δH 4.94 and 5.32 ppm (2:1 ratio), while the ¹³C NMR spectrum contains signals at δC 53.13 and 68.23 ppm assigned to the carbon atoms located between two nitrogen atoms and the sulfur and nitrogen atoms, respectively.

CYCLOMETHYLATION OF p-ANILINE SULFAMIDE AND ITS DERIVATIVES

We investigated cyclothiomethylation of p-aminosulfanyl acid amides, namely, p-aniline sulfamide 1g, p-aminobenzene sulfacetamide 1h, 2-(p-aminobenzenesulfamido)-3-methoxypyrazine and 4-(p-aminobenzenesulfamido)-2,6-dimethoxypirimidine with the aid of CH₂O and H₂S.

Condensation of p-aniline sulfamide 1g was carried out (1g:CH₂O:H₂S = 1:3:2) under different temperature conditions (0-80 °C). It was stated that cyclothiomethylation of p-aniline sulfamide 1g within the temperature range from 0 to 40 °C gave rise to the dithiazinane cycle formation exclusively involving the amino group of the aromatic ring to obtain 4-(1,3,5-dithiazinane-5-yl)aniline sulfamide 2g in 35-73% yield (Scheme 3, Table 1). The increase the temperature to 80 °C facilitates the involvement of less reactive SO₂NH₂ into the cyclocondensation reaction. So, in these experiments together with 2g cyclodimer 4g. The obtained mixture of compounds 2g and 4g (3:1 ratio) was divided by fractional crystallization (Scheme 3).

Scheme 3. Cyclothiomethylation of p-aniline sulfamide
Cryoscopic determinations with a value of 285±10 correspond to the molecular weight (mass) of compound 2g, and a value of 493±10 corresponds to the molecular weight of macroheterocycle 4g. The element analysis of compound 2g confirms the molecular formula C₉H₁₂N₂O₂S₃ and the molecular formula C₁₆H₂₀N₄O₄S₄ for compound 4g as well.

To obtain 1,3,5-dithiazinanes simultaneously involving of both amino groups of p-aniline sulfamide 1g into the reaction with CH₂O and H₂S, we have increased a quantity of a thiomethylation mixture: 1g:CH₂O:H₂S = 1:6:4 (0, 20, 40, and 80 °C). As a result, cyclocondensation proceeded via both NH₂ groups to give the four-component mixture, GC/MS spectrum of which contains peaks of molecular ions of the characteristic residual fragments with \( m/z \) 318 (7g), 334 (6g), 364 (8g) and 380 (5g), apparently corresponding to compounds with the (oxy)thiazethidine 6g,7g and (oxy)dithiazinane 5g,8g cycles.

Cyclocondensation of 1g by a mixture of CH₂O and H₂S (1g:CH₂O:H₂S = 1:6:4) in acid medium (pH 1.3-1.5) at 40 °C led to the formation of 5-[4-(1,3,5-dithiazinane-5-sulfonyl)phenyl]-1,3,5-dithiazinane 5g in 93% yield and with 100% selectivity (Scheme 3, Table).

Table. The influence of pH medium and initial reagent ratio on the yield and product content of p-aniline sulfamide 1g cyclomethylation

<table>
<thead>
<tr>
<th>Reagent ratio 1g:CH₂O:H₂S</th>
<th>pH</th>
<th>T, °C</th>
<th>Yield (%)</th>
<th>2g</th>
<th>4g</th>
<th>5g</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:3:2</td>
<td>7.3-7.4</td>
<td>0</td>
<td>35</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>7.3-7.4</td>
<td>20</td>
<td>58</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>7.3-7.4</td>
<td>40</td>
<td>73</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>7.3-7.4</td>
<td>80</td>
<td>52</td>
<td>14</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1:6:4</td>
<td>1.3-1.5</td>
<td>40</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>93</td>
</tr>
</tbody>
</table>

The ¹H NMR spectrum of heterocycle 2g exhibits proton signals of aromatic ring at \( \delta_H \) 6.80-7.67 ppm. Singlet signals at \( \delta_H \) 3.82 and 4.32 ppm correspond to methylene protons located between the sulfur atoms and atoms of N and S, respectively, with integrated intensity of 1:2. The ¹³C NMR spectrum for 2g contains signals of the carbon atoms in aromatic rings at \( \delta_C \) 116.48, 127.12, 133.99, and 147.86 ppm. The signals at \( \delta_C \) 32.96 and 53.30 ppm evidences the presence of the dithiazinane ring methylene groups in compound 2g.
The $^1$H NMR spectrum of heterocycle 4g exhibits proton signals of aromatic ring at $\delta$H 6.73-7.11 ppm. The singlet signals, which correspond to the methylene protons between the nitrogen and sulfur atoms, appeared at 3.98 and 4.52 ppm at a ratio of 1:1. The proton signals at $\delta$H 7.54 and 7.63 ppm belong to NH group. The $^{13}$C NMR spectrum of compound 4g contains the carbon atom signals of aromatic rings at $\delta$C 112.73, 127.35, 131.91, and 149.39 ppm. The presence of signals at $\delta$C 44.74 and 63.49 ppm for 4g characterizes the presence of CH$_2$ groups between N and S atoms.

In $^1$H NMR spectrum of compound 5g the protons of aromatic ring are observed at $\delta$H 6.73-8.02, the methylene protons of SCH$_2$S and SCH$_2$N groups of the dithiazinane ring, linked with aromatic ring, are observed at $\delta$H 3.93 and 4.72 ppm (1:2 ratio), and of sulfo group at $\delta$H 4.26 and 5.14 ppm, respectively. The $^{13}$C NMR spectrum of compound 5g exhibits the signals of dithiazinane cycle carbon atoms, bound with aromatic ring, at $\delta$C 31.48 and 56.05 ppm, and with sulfo group at $\delta$C 33.10 and 63.40 ppm.

Cyclothiomethylation of $p$-aniline sulfacetamide 1h was found to proceed simultaneously via NH$_2$ and SO$_2$(Ac)NH groups in acid medium ($p$H 2.5). Under these conditions cyclodimer 4h has been obtained in 50% yield as a result of intermolecular condensation of two molecules of 1h with a thiomethylation reagent CH$_2$O-H$_2$S (Scheme 5) with 70% conversion. In neutral and alkaline medium, $p$-aniline sulfacetamide 1h did not react with CH$_2$O and H$_2$S and 1,2,4-trithiolane was predominantly formed.8

![Scheme 4. Cyclothiomethylation of $p$-aniline sulfo acetamide](image)

The molecular weight of 543.53±10 (calc. M$_{cr}$ 544) determined by Rast cryoscopy method7 and the data of element analysis correspond to molecular formula C$_{20}$H$_{24}$N$_4$O$_6$S$_4$ that proved the formation of macroheterocycle 4h. The $^1$H NMR spectrum shows signals of methylene sulfide protons connected with amino group at $\delta$H 4.50 ppm, and connected with the sulfo acetamide group at $\delta$H 5.11 ppm. The $^{13}$C NMR spectrum contains signals at $\delta$C 43.61 and 44.28 ppm assigned to carbon atoms of CH$_2$NH and CH$_2$NSO groups, respectively.

Cyclocondensation of [(($p$-aniline)sulfamido]-3-methoxypyrazine and [4-($p$-aniline)sulfamido]-2,6-dimethoxypyrimidine containing pyrimidine rings under conditions described above does not proceed with CH$_2$O H$_2$S. The low activity of NH$_2$ group in compounds 1i and 1k is, apparently, connected with the formation of the intermolecular hydrogenous bonds between NH$_2$ group and the nitrogen atoms of pyrimidine ring.
In conclusion, cyclocondensation of o- (1a), p- (1b) aminobenzoic, 4- (1c), 5- (1d) aminosalicylic acids, ethyl- (1e), (β-diethylamino)ethyl esters- (1f) of p- (1b) and p-aniline sulfamide 1g with CH₂O and H₂S under optimized conditions leads to the formation of the corresponding ditiazinanes 2a-g, whereas p-aminobenzoic 1b, 5-aminosalicylic acid 1d and p-aminobenzoic acid ethyl ester 1e together with dithiazinanes give rise to thiazetidines. Cyclothiomethylation of p-aminobenzoic acid ethyl ester by the CH₂O-H₂S reagent at 0 °C was found to afford N,N-diaryl-1,3,5-thiadiazinane 4e in quantitative yield (93%). The reaction for obtaining bis-1,3,5-dithiazinanes 5g (93%) from p-aniline sulfamide 1g are more effective in acid medium (pH 1.3-1.5) at 40 °C. It was shown that in the cyclothiomethylation at 80 °C together with the formation of dithiazinane (56%) p-aniline sulfamide 1g undergoes intermolecular condensation to give cyclodimer 4g (14%). The analogous intermolecular cyclocondensation of p-aniline sulfacetamide in acid medium (pH 2.5) leads to cyclodimer 4h (50%) built from two fragments of p-aniline sulfacetamide linked by sym dimethyl sulfide chain (CH₂SCH₂).

EXPERIMENTAL

All solvents were freshly distilled. The 1H NMR spectra of compounds 2a-g, 3b-d,e and 4g, 5g were measured on spectrometer “Tesla BS-487”, 13C NMR - on spectrometer Jeol FX 90Q (22.50 MHz), internal standard - Me₄Si. NMR experiments of compounds 4e and 4h were recorded on a Bruker AVANCE-400 spectrometer. The GLC-mass spectrometry was carried out on Finigan 4021 instrument. The IR-spectra were recorded on Specord 75 IR in spectrophotometer in Nujol mulls. Elemental analysis of C, H, N, S samples was determined on element analysator of Karlo Erba, model 1106. The pH values of solutions were determined on a pH meter (pH – 340). Melting points were determined on Kofler unit. Column chromatography was performed with the use of silica gel.

Single-crystal X-ray diffraction experiments were carried out with a Bruker SMART 1000 CCD area detector, using graphite monochromated Mo-Kα radiation at 100 K. All calculations were performed on an IBM PC/AT using the SHELXTL software [G. M. Sheldrick, SHELXTL-97, Version 5.10, Bruker AXS Inc., Madison, WI-53719, USA]. Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC), deposition numbers 679451 (4e).

Cyclothiomethylation of functional substituted anilines (1a-1h). The calculated amount of 37% formalin (1.1 mL, 0.015 mol) or (2.2 mL, 0.030 mol) were charged to a three-neck flask equipped with a stirrer and barbotager thermostated at the chosen temperature. Hydrogen sulfide (prepared in excess amount from Na₂S and HCl) was barbotaged to give CH₂O–H₂S mixture at a ratio of 3:2 or 6:4. Then calculated amount of anylines (1a, 1b, 1c, 1d, 1e, 1f, 1g or 1h; 0.005 mol) was added to the reaction mixture. The mixture was stirred for 2-3 h at a chosen temperature. Compounds 2e, 3e, 4e were isolated.
by column chromatography with C₆H₆/EtOAc (10:1) as the eluent. The products 2a–d, 3b, 3d, 2g, 4g were selected by fractional crystallization from CHCl₃. Compounds 5g and 4h were filtered.

7-(1,3,5-Dithiazinane-5-yl)-2-benzoic acid (2a). White powder (61%). mp 159-160 °C. m/z (%): 241 (5) [M]+, 197 (47), 163 (5), 150 (30), 120 (53), 105 (5), 92 (44), 77 (12), 61 (100). ¹H NMR (80 MHz, DMSO-d₆): δ (ppm) 3.75 (s, 2H, 2H-2), 4.66 (s, 4H, 2H-4, 2H-6), 6.64-7.00 (m, 2H, H-10, H-12), 7.28-7.53 (m, 2H, H-9, H-11), 8.00 (s, H, H-15). ¹³C NMR (22.5 MHz, DMSO-d₆): δ (ppm) 32.2 (C-2), 44.5 (C-6, C-4), 109.9 (C-8), 114.9 (C-10), 116.6 (C-12), 131.5 (C-9), 134.0 (C-11), 151.7 (C-7), 169.9 (C-13). IR (KBr): 750, 1230, 1600, 1660, 2900, 3320 cm⁻¹. Anal. Calcd for C₁₀H₁₁O₂NS₂: C 49.79, H 4.56, N 5.80, S 26.55. Found: C 50.11, H 4.60, N 5.79, S 26.46.

7-(1,3,5-Dithiazinane-5-yl)-4-benzoic acid (2b). White powder (95%). mp 227-229 °C. m/z (%): 241 (9) [M]+, 207 (12), 91 (15); 44 (100). ¹H NMR (80 MHz, DMSO-d₆): δ (ppm) 4.00 (d, J=8.0 Hz, 2H, 2H-2), 4.64 (br. s, 4H, 2H-4, 2H-6), 6.72 (d, J=8.0 Hz, 2H, H-8, H-12), 7.17 (d, J=8.0 Hz, 2H, H-9, H-11), 7.83 (s, H, H-13). ¹³C NMR (22.5 MHz, DMSO-d₆): δ (ppm) 33.7 (C-2), 56.3 (C-6, C-4), 113.8 (C-8, C-12), 121.0 (C-10), 131.0 (C-9, C-11), 149.1 (C-7), 167.7 (C-13). IR (KBr): 780, 1200, 1600, 1680, 2900, 3300 cm⁻¹. Anal. Calcd for C₁₀H₁₁O₂NS₂: C 49.79, H 4.56, N 5.80, S 26.55. Found: C 49.79, H 4.56, N 5.79, S 26.63.

5-(1,3-Thiazetidine-3-yl)-4-benzoic acid (3b). White powder (51%). mp 209-210 °C. m/z (%): 195 (52) [M]+, 150 (33); 120 (57), 105 (5), 92 (44), 77 (12), 61 (100). ¹H NMR (80 MHz, DMSO-d₆): δ (ppm) 4.36 (br. s, 4H, 2H-2, 2H-4), 6.72 (d, J=8.0 Hz, 2H, H-6, H-10), 7.17 (d, J=8.0 Hz, 2H, H-7, H-9), 7.83 (s, H, H-13). ¹³C NMR (22.5 MHz, DMSO-d₆): δ (ppm) 53.3 (C-2, C-4), 116.4 (C-6, C-10), 120.0 (C-8), 131.0 (C-7, C-9), 147.2 (C-5), 167.7 (C-11). IR (KBr): 780, 1200, 1600, 3300 cm⁻¹. Anal. Calcd for C₉H₉O₂NS: C 55.38, H 4.61, N 7.17, S 16.41. Found: C 55.53, H 4.59, N 7.29, S 16.92.

4-(1,3,5-Dithiazinane-5-yl)-2-hydroxybenzoic acid (2c). White powder (89%). mp 258-260 °C. ¹H NMR (80 MHz, DMSO-d₆): δ (ppm) 4.06 (s, 2H, 2H-2), 5.20 (s, 4H, 2H-4 and 2H-6), 6.23 (s, H, H-12), 6.70 (s, H, H-8), 7.85 (s, H, H-11), 8.50 (br. s, 2H, H-13, H-14). ¹³C NMR (22.5 MHz, DMSO-d₆): δ (ppm) 33.6 (C-2), 53.2 (C-4, C-6), 103.7 (C-10), 106.4 (C-8), 108.4 (C-12), 131.4 (C-11), 151.5 (C-7), 163.1 (C-9), 172.3 (C-13). IR (KBr): 720, 1170, 1450, 1600, 1660, 2900, 3360 cm⁻¹. Anal. Calcd for C₁₀H₁₁O₃NS₂: C 46.69, H 4.42, N 5.44, S 24.90. Found: C 47.21, H 4.33, N 5.48, S 25.16.

5-(1,3,5-Dithiazinane-5-yl)-2-hydroxybenzoic acid (2d). White powder (32%). mp 194-196 °C. ¹H NMR (80 MHz, DMSO-d₆): δ (ppm) 4.00 (s, 2H, 2H-2), 5.20 (s, 4H, 2H-4 and 2H-6), 6.23 (s, H, H-12), 6.70 (s, H, H-8), 7.85 (s, H, H-11), 8.50 (br. s, 2H, H-13, H-14). ¹³C NMR (22.5 MHz, DMSO-d₆): δ (ppm) 33.5 (C-2), 56.9 (C-4, C-6), 113.0 (C-9), 114.7 (C-11), 117.9 (C-8), 123.0 (C-12), 137.7 (C-7), 155.0 (C-10), 171.8 (C-14). IR (KBr): 800, 1190, 1440, 1600, 1660, 2900 cm⁻¹. Anal. Calcd for C₁₀H₁₁O₃NS₂: C 46.69, H 4.42, N 5.44, S 24.90. Found: C 46.73, H 4.27, N 5.54, S 25.00.
5-(1,3-Thiazetidine-3-yl)-2-hydroxybenzoic acid (3d). White powder (22%). mp 164-166 °C. 1H NMR (80 MHz, DMSO-d6): δ (ppm) 4.35 (s, 4 H, 2H-2, 2H-4), 6.80-7.50 (m, 3 H, H-6, H-9, H-10) 8.47 (br, s, 2 H, H-11, H-12). 13C NMR (22.5 MHz, DMSO-d6): δ (ppm) 54.5 (C-2, C-4), 113.0 (C-7), 115.1 (C-9), 119.2 (C-6), 126.3 (C-10), 138.1 (C-5), 158.8 (C-8), 172.2 (C-12). IR (KBr): 800, 1190, 1440, 1600, 1660, 2900 cm⁻¹. Anal. Calcd for C10H9O2NS: C 51.17, H 4.29, N 6.63, S 15.18. Found: C 51.53, H 4.36, N 6.42, S 15.03.

Ethyl-4-(l,3,5-dithiazinan-5-yl)benzoate (2e). White powder (56%). mp 136-138 °C. m/z (%) = 269 (40) [M]+, 191 (21), 177 (70), 163 (24), 149 (33), 132 (100), 77 (36) 45 (52). 1H NMR (80 MHz, CDCl3): δ (ppm) 1.38 (t, J=7.2 Hz, 3 H, H3-C-16), 3.92 (s, 2 H, 2H-2), 4.30 (s, 4 H, 2H-4, 2H-6), 5.10 (br, s, 2 H, 2H-15), 7.05 (d, J=9.0 Hz, 2 H, H-8, H-12), 8.05 (d, J=9.0 Hz, 2 H, H-9, H-11). 13C NMR (22.5 MHz, CDCl3): δ (ppm) 14.3 (C-16), 34.8 (C-2), 54.5 (C-4, C-6), 60.4 (C-15), 116.2 (C-8, C-12), 121.9 (C-10), 131.0 (C-9, C-11), 148.5 (C-7), 164.6 (C-13). IR (KBr): 750, 1230, 1450, 1660, 3320 cm⁻¹. Anal. Calcd for C12H15O2NS: C 53.53, H 5.58, N 5.20, S 23.79. Found: C 54.19, H 5.48, N 5.11, S 23.77.

Ethyl-4-(l,3-thiazetidin-3-yl)benzoate (3e). White powder (18%). mp 175-177 °C. m/z (%) = 225 (0.4) 223 (9) [M]+, 177 (9), 150 (15), 149 (100), 132 (15), 44 (42), 46 (1.7). 1H NMR (80 MHz, CDCl3): δ (ppm) 1.34 (t, J=7.2 Hz, 3 H, H3-C-14), 4.25 (k, J= 9.0 Hz, 2 H, H2-C-13), 5.10 (br, s, 4H, 2H-2, 2H-4), 6.98 (d, J=6.3 Hz, 2 H, H-6, H-10), 7.68 (d, J=6.3 Hz, 2 H, H-7, H-9). 13C NMR (22.5 MHz, CDCl3): δ (ppm) 14.4 (C-14), 53.2 (C-2, C-4)), 60.6 (C-13), 116.4 (C-10, C-6), 125.5 (C-8), 131.2 (C-7, C-9), 155.0 (C-5), 165.6 (C-11). IR (KBr): 750, 1230, 1450, 1660, 3320. Anal. Calcd for C11H13O2NS: C 59.19, H 5.83, N 6.28, S 14.35. Found: C 57.20, H 5.42, N 6.11, S 15.77.

3,5-Di-(4-ethylcarboxyphenyl)-l,3,5-thiadiazinane (4e). Compound 4e was isolated by column chromatography (yield 15%). And also the compound 4e has selectively been received at 0 °C, the starting reagents were taken in the ratio 1e:CH2O·H2S = 2:3:1 (yield 93%). White powder, mp 184-186 °C. 1H NMR (400 MHz, CDCl3): δ (ppm) 1.32 (t, J=6.5 Hz, 6 H, H3-C-22, H3-C-26), 4.24 (d, J=6.8 Hz, 4 H, 2H-21, 2H-25), 4.94 (s, 4 H, 2H-2, 2H-6), 5.32 (s, 2 H, 2H-4), 6.91 (d, J=8.1 Hz, 4 H, H-8, H-12, H-14, H-18), 7.79 (d, J=8.1 Hz, 4 H, H-9, H-11, H-15, H-17). 13C NMR (100 MHz, CDCl3): δ (ppm) 14.4 (C-22, C-26), 53.1 (C-2, C-6), 60.57 (C-25, C-21), 68.2 (C-4), 116.3 (C-12, C-8, C-18, C14), 122.1 (C-16, C-10), 131.2 (C-11, C-9, C-17, C-15), 150.5 (C-7, C-13), 166.4 (C-23, C-19). IR (KBr): 750, 1230, 1450, 1660, 3320. Anal. Calcd for C13H15O2NS: C 62.98, H 5.04, N 6.99, S 8.01. Found: C 63.25, H 5.32, N 7.11, S 8.65.

4-(1,3,5-Dithiazinane-5-yl)-2-(diethylamino)ethylbenzoate (2f). White powder (79%). mp 51-52 °C. 1H NMR (80 MHz, CDCl3): δ (ppm) 0.45 (t, J=6.3 Hz, 6 H, H3-C-19, H3-C-22), 1.30 (t, J=9.0Hz, 2 H, 2H-16), 3.12 (k, J=10.1 Hz, 4 H, 2H-18, 2H-21), 3.80 (t, J=9.0 Hz, 2 H, 2H-15), 4.22 (s, 2 H, 2H-2), 4.68 (s, 4 H, 2H-4, 2H-6), 7.3 (br, s, 2H, H-8, H-12), 7.87 (s, 2 H, H-9, H-11). 13C NMR (22.5 MHz, CDCl3): δ (ppm)
8.5 (C-19, C-22), 32.4 (C-2), 47.1 (C-18, C-21), 49.5 (C-4, C-6), 53.8 (C-16), 58.2 (C-15), 116.9 (C-8, C-12), 131.1 (C-9, C-11), 150.5 (C-7), 164.5 (C-13). IR (KBr): 770, 1100, 1380-1450, 1600, 1680, 2900 cm\(^{-1}\). Anal. Calcd for C\(_{16}H_{24}O_2N_2S_2\): C 56.47, Н 8.24, N 8.24, S 18.82. Found: C 51.97, Н 7.46, N 7.70, S 19.50.

4-(1,3,5-Dithiazinane-5-yl)benzenesulfonamid (2g). White powder (73%). mp 135-137 °C. \(^1\)H NMR (80 MHz, DMSO-\(d_6\)): \(\delta\) (ppm) 3.90 (s, 2 H, 2H-2), 4.56 (s, 4 H, 2H-4, 2H-6), 5.16 (s, 2 H, 2H-14), 6.80 (d, \(J=8.3\) Hz, 2H, H-8, H-12), 7.67 (d, \(J=8.3\) Hz, 2 H, H-9, H-11). \(^1\)C NMR (22.5 MHz, DMSO-\(d_6\)): \(\delta\) (ppm) 33.0 (C-2), 53.3 (C-4, C-6), 116.5 (C-8, C-12), 127.1 (C-9, C-11), 134.0 (C-7), 147.9 (C-10). IR (KBr): 685, 820, 1090, 1140, 1305, 1450, 1600, 2905, 3365 cm\(^{-1}\). Anal. Calcd for C\(_9H_{12}N_2S_3O_2\): С 39.11, Н 4.38, N 10.14, S 34.80. Found: C 39.47, Н 4.84, N 11.84, S 35.67.

2,2,12,12-Tetraon-2λ₆,5,12λ₆,15-tetrathia-3,7,13,17-tetraazatricyclo[16.2.2.2₈,₁₁]-tetracosa-1(20),8,10,18,21,23-hexaene (4g). White powder (14%). mp 146-148 °C. \(^1\)H NMR (80 MHz, DMSO-\(d_6\)): \(\delta\) (ppm) 3.98 (s, 4 H, 2H-6, 2H-16), 4.52 (s, 4 H, 2H-4, 2H-14), 6.73 (d, \(J=8.44\) Hz, 4 H, H-9, H-22, H-19, H-23), 7.11 (d, \(J=8.44\) Hz, 4 H, H-10, H-20, H-22, H-24), 7.54 (m, 2 H, NH-7, NH-17), 7.63 (s, 2 H, NH-3, NH-13). \(^1\)C NMR (22.5 MHz, DMSO-\(d_6\)): \(\delta\) (ppm) 44.7 (C-6, C-16), 63.5 (C-4, 14), 112.7 (C-9, C-19, C-21, C-24), 127.4 (C-10, C-20, C-22, C-23), 131.9 (C-8, C-18), 149.4 (C-1, C-11). IR (KBr): 560, 815, 1095, 1150, 1305, 1460, 1600, 2910, 3370 cm\(^{-1}\). Anal. Calcd for C\(_{16}H_{20}N_4S_4O_4\): С 41.72, Н 4.38, N 12.16, S 27.85. Found: C 39.35, Н 4.54, N 11.82, S 33.73.

5-[4-(1,3,5-Dithiazinan-5-ylsulfonyl)phenyl]-1,3,5-dithiazinane (5g). Analogously to the above-described procedure compound (5g) was prepared with accompaniment of the 0.01 mol HCl. After 2 h the reaction mixture was neutralized with an aqueous KOH solution. White powder (93%). mp 154-156 °C. \(^1\)H NMR (80 MHz, DMSO-\(d_6\)): \(\delta\) (ppm) 3.93 (s, 2 H, 2H-2), 4.26 (s, 2 H, 2H-17), 4.72 (s, 4 H, 2H-4, 2H-6), 5.14 (s, 4 H, 2H-15, 2H-19), 6.73 (d, \(J=7.98\) Hz, 2 H, H-9, H-12), 8.02 (d, \(J=7.98\) Hz, 2 H, H-11). \(^1\)C NMR (22.5 MHz, DMSO-\(d_6\)): \(\delta\) (ppm) 31.5 (C-2), 33.1 (C-17), 56.1 (C-4, C-6), 63.4 (C-15, C-19), 114.0 (C-8, C-12), 127.0 (C-9, C-11), 128.0 (C-10), 146.6 (C-7). IR (KBr): 645-695, 1005, 1095, 1105, 1140, 1305, 1460, 1600, 2910, 3370 cm\(^{-1}\). Anal. Calcd for C\(_{16}H_{16}N_2S_5O_2\): C 37.87, Н 4.24, N 7.36, S 42.13. Found: C 37.71, Н 4.53, N 8.18, S 43.91.

5-[4-(1,3-Thiazetan-3-ylsulfonyl)phenyl]-1,3,5-dithiazinane (6g). White powder (20%). \(m/z\) (%): 334 (5) [\(M^+\)], 156 (15), 108 (35), 43 (50). IR (KBr): 550, 1005, 1090, 1140, 1300, 1445, 1595, 2900 cm\(^{-1}\).

5-[4-(1,3-Oxazetan-3-ylsulfonyl)phenyl]-1,3,5-dithiazinane (7g). White powder (20%). \(m/z\) (%): 318 (5) [\(M^+\)], 156 (12), 108 (40), 76 (24), 43 (95). IR (KBr): 550, 1005, 1140, 1300, 1445, 1595, 2900 cm\(^{-1}\).

5-[4-(1,3,5-Oxathiazinan-5-ylsulfonyl)phenyl]-1,3,5-dithiazinane (8g). White powder (20%). \(m/z\) (%): 364 (2) [\(M^+\)], 200 (20), 136 (60), 78 (30), 43 (100). IR (KBr): 550, 810, 1090, 1300, 1445, 2900 cm\(^{-1}\).
tetracosa-1(20),8,10,18,21,23-hexaene (4h). Analogously to the above-described procedure compound (4h) was prepared with accompaniment of the 0.01 mol HCl. After 3h the reaction mixture was neutralized with an aqueous KOH solution. White powder (51%). mp 126-127 °C. ¹H NMR (400 MHz, DMSO-d₆): δ (ppm) 1.88 (s, 6 H, Н₃С-26, Н₃С-28), 4.5 (s, 4 H, 2H-6, 2H-16); 5.11 (s, 4 H, 2H-4, 2H-14); 6.73 (d, J = 6.85, 4 H, H-9, H-23, H-19, H-22); 7.63 (d, J = 6.85, 4 H, H-10, H-24, H-20, H-21); 21 (m, 2 H, Н-7, Н-17). ¹³C NMR (100 MHz, DMSO-d₆): δ (ppm) 23.4 (C-26, C-28), 43.6 (C-6, C-16); 44.3 (C-4, C-14); 116.3 (C-9, C-19, C-22, C-24); 129.6 (C-20, C-21, C-10, C-24), 147.4 (C-1, C-11), 153.8 (C-8, C-18), 169.0 (C-25, C-27). IR (KBr): 770, 1100, 1400-1450, 1570, 1620, 2900 cm⁻¹.


REFERENCES


