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CYCLOTHIOMETHYLATION OF FUNCTIONAL SUBSTITUTED ANILINES BY CH_2O AND H_2S

Vnira R. Akhmetova,[1*] Guzel R. Nadyrgulova,[1] Zalifa T. Niatshina,[2] Regina R. Khairullina,[1,2] Zoya A. Starikova,[3] Alexandra O. Borisova,[3] Michail Yu. Antipin,[3] Raihana V. Kunakova,[2] and Usein M. Dzhemilev[1]

[1]Institute of Petrochemistry and Catalysis, RAS, 450075 Ufa, Prospekt Oktyabrya, 141, Russian Federation, e-mail address: ink@anrb.ru. [2]Ufa State Academy of Economy and Service, 450077 Ufa, Chernyshevskii Street, 145, Russian Federation, e-mail address: utis@bashnet.ru. [3]A.N. Nesmeyanov Institute of Elementoorganic Chemistry, RAS, 11999 Moscow, Vavilov Street, 28, Russian Federation, e-mail address: star@xray.ineos.ac.ru

Abstract – *N*-Aryl substituted 1,3,5-dithiazinanes 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 CH_2O and H_2S (1:3:2 ratio). At ambient temperature *p*-aminobenzoic acid, 5-aminosalicylic acid and *p*-aminobenzoic acid ethyl ester together with 1,3,5-dithiazinanes form appropriate *N*-aryl substituted 1,3-thiazetidines. Cyclothiomethylation of *p*-aminobenzoic acid ethyl ester (0 °C) results in *N,N*-diaryl-1,3,5-thiadiazinane. Heterocyclization of *p*-aniline sulfamide with CH_2O and H_2S at a molar ratio of 1:6:4 (pH 1.3–1.5) was found to afford *bis*-1,3,5-dithiazinanes involving two amino groups. Condensation of *p*-aniline sulfacetamide with 37% formalin (CH_2O) and H_2S (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 (CH_2SCH_2).

INTRODUCTION

In organic chemistry there is an original method for the synthesis of 1,3,5-dithiazinane[1a-e] based on Wohl reaction namely multimolecular cyclocondensation of methyl amine, 37% formalin (CH_2O) and H_2S. Compounds, which contain dithiazinane ring, are used as insecticides and fungicides[2a,b] as well as

additives modified and intensified product taste,[2c-g] inhibitors, ferments,[2h] complexons,[3a-g] sorbents for gold and silver.[4a,b]

For the last 5 years we systematically investigated the Wohl reaction using cyclothiomethylation of aliphatic[5a] and aromatic[5b] amines, amino acids,[5c] aminoalcohols[5d] aminophenols[5e] as an example to obtain the corresponding *N*-substituted 1,3,5-dithiazinanes,[5a-e] 1,3-thiazetidines[5a,b,c] and 1,3,5-thiadiazinanes.[5b] The direction of the cyclothiomethylation reaction depends on the structure of initial amines and reaction conditions (ratio and order of reagent mixing,[5a,c] temperature,[5a-e] medium *p*H), under which cyclocondensation is conducted. Thus, it was shown that in the cyclothiomethylation reaction of aliphatic[5a] and aromatic[5b] amines with CH_2O and H_2S (amine: CH_2O: H_2S = 1:3:2) the decrease in basicity of amines causes the increase in the yield of target 1,3,5-dithiaz inanes. Further more thorough and deep analysis of cyclocondensation of functionally-substituted anilines, namely *o-, m-* and *p*-aminophenols, with CH_2O and H_2S has shown, that the direction of the cyclothiomethylation reaction of aminophenols depends on the position of functional amino group.[5e] Aminophenols, *o*- and *p*-isomers, were established to interact with CH_2O and H_2S as a reactant mixture (3:2 ratio) to form 1,3,5-dithiazinanes. *m*-Aminophenol under analogous conditions undergoes intermolecular condensation with CH_2O and H_2S 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_2O and H_2S 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-dithiazinanes, 1,3,5-thiadiazinanes and macroheterocycles.

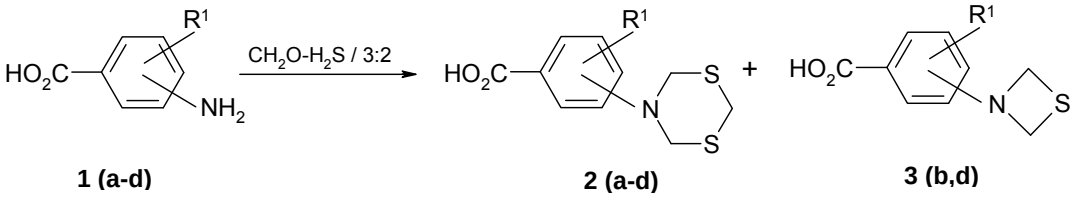
RESULTS AND DISCUSSION

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

In cyclocondensation with CH_2O and H_2S 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 (*β*-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_2O and H_2S (1:3:2 ratio) at 20 °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.



1 (a-d) **2 (a-d)** **3 (b,d)**

2 -NH_2 ,R^1 = H (**a**), 4 -NH_2 , R^1 = H (**b**), 4 -NH_2 , R^1 = 2-OH (**c**), 5 -NH_2 , R^1 = 2-OH (**d**)

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_2O and H_2S 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.

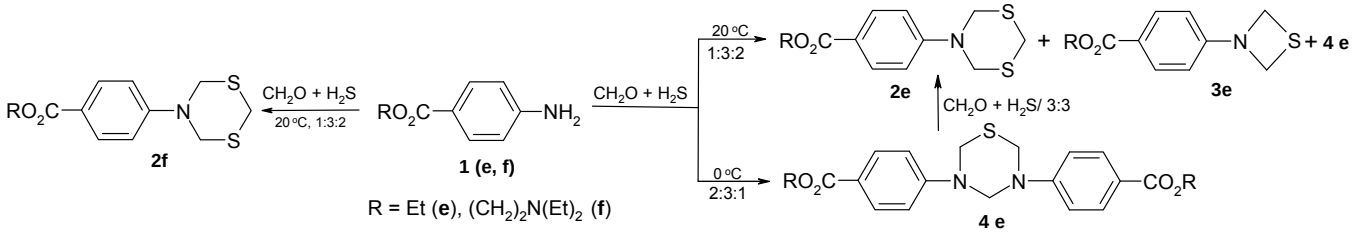
4-Aminosalicylic acid **1c**, in which OH and NH_2 groups occupy *meta*- position, in contrast to *m*-aminophenol, reacts with CH_2O and H_2S exclusively at the amino group, probably, as a result of the intramolecular hydrogen bonding between OH and COOH groups (OH... O the *ortho*-effect).[6] As is evident, the direction of cyclothiomethylation of isomeric aromatic amino acids with the aid of CH_2O and H_2S 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: ^{1}H NMR and ^{13}C NMR, GC/MS, and also by the data of element analysis. Molecular weight was determined by Rast cryoscopic method.[7] Heterocycle **2a** was obtained earlier[4a] with 81% yield by cyclocondensation of **1a** with NaHS and CH_2O, for which any spectral characteristics were absent.

Thus, aromatic amino acids were condensed with CH_2O and H_2S only at NH_2 group with the formation of *N,S*-containing heterocycles (1,3,5-dithiazinanes and 1,3-thiazetidines). One should notice that *para*-position of COOH group contributes to an increase of NH_2 group activity in the condensation reaction with CH_2O and H_2S. 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.[8]

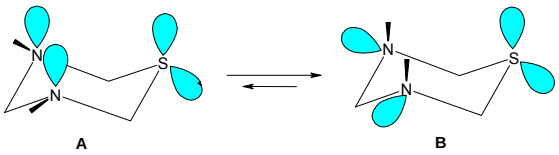
By the reaction of *p*-aminobenzoic acid ethyl **1e** or (*β*-diethylamino)ethyl **1f** esters with CH_2O and H_2S (1:3:2 ratio) at 20 °C the compounds of dithiazinane row **2e,f** has been obtained. Amino ester **1e** in this reaction together with ethyl-4-(1,3,5-dithiazinan-5-yl) benzoate **2e** gave 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 CH_2O and H_2S (2:3:1 ratio) in 93% yield. Heterocyclic **4e** in the presence of three-molar excess of a thiomethilation mixture CH_2O-H_2S 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).[9a,b]

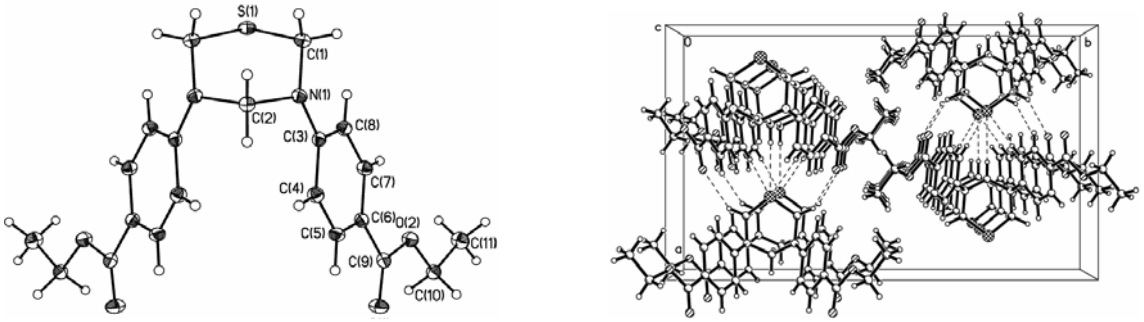


Figure. General view (a) and fragment of crystal packing (b) of compound **4e** in the crystal

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

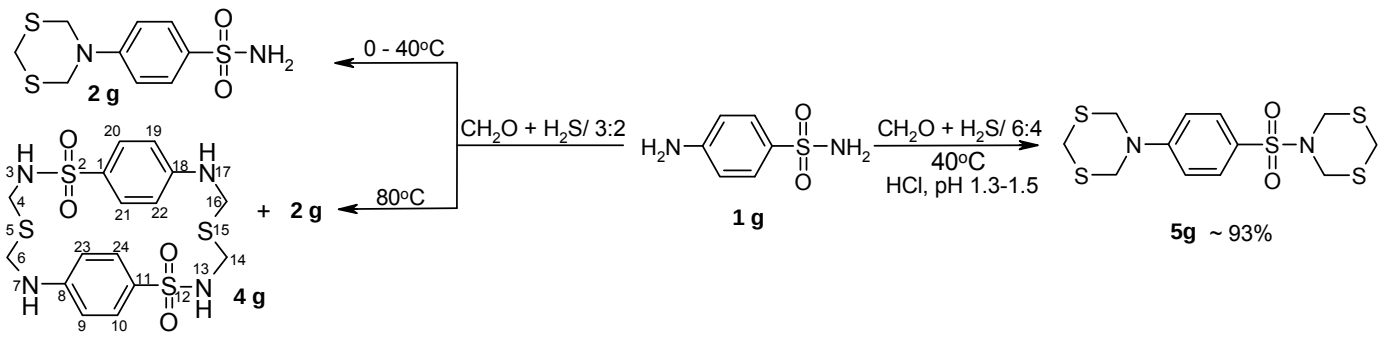
rings at C(4) and with methylene protons of another thiadiazinane molecule at C(2): HC(4)…S(1)…HC(4') и HC(2)...S(1) (where H.. S distances are equal to 2.83Å (x 2) and 2.78Å, respectively). At the same time, the ester carbonyl groups of the first thiadiazinane molecule are connected with methylene protons of two other thiadiazinane molecules: O(1)…HC(1A) and O(1')…HC(1B) (distances O.. H 2.54Å (x 2)).

In the ^{1}H NMR spectra of dithiazinane cycles **2a-f** one could observe two singlets of methylene protons at δ_H 3.40-4.22 (SCH_2S) and 4.15-5.20 ppm (NCH_2S) with integrated intensities ratio of 1:2. The ^{13}C NMR spectra contain signals at δ_C 30.61-34.80 (SCH_2S) and 44.51-56.89 ppm (NCH_2S) belonging to the carbon atoms. The ^{1}H NMR spectrum of thiazetidine cycle (compounds **3b,d,e)** exhibits singlets of methylene protons (NCH_2S) at δ_H 4.30-5.15 ppm, while the ^{13}C NMR spectra contain peaks at δ_C 51.97-54.60 ppm. In the ^{1}H NMR spectra of thiadiazinane **4e** the signals for CH_2SCH_2 and NCH_2N methylene protons are observed at δ_H 4.94 and 5.32 ppm (2:1 ratio), while the ^{13}C NMR spectrum contains signals at δ_C 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 CH_2O and H_2S.

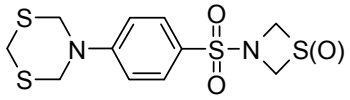
Condensation of *p*-aniline sulfamide **1g** was carried out (**1g**: CH_2O: H_2S = 1:3:2) under different temperature conditions (0-80 °C). It was stated that cyclothiomethylation of *p*-aniline sulfamide **1g** within the temperature range from 0 to 40 °C gave rise to the dithiazinane cycle formation 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 SO_2NH_2 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).



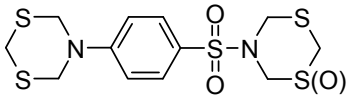
Scheme 3. Cyclothiomethylation of *p*-aniline sulfamide

Cryoscopic determinations[7] 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 $C_9H_{12}N_2O_2S_3$ and the molecular formula $C_{16}H_{20}N_4O_4S_4$ 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 CH_2O and H_2S, we have increased a quantity of a thiomethylation mixture: **1g**: CH_2O: H_2S = 1:6:4 (0, 20, 40, and 80 °C). As a result, cyclocondensation proceeded via both NH_2 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.



6g,7g



5g,8g

Cyclocondensation of **1g** by a mixture of CH_2O and H_2S (**1g**: CH_2O: H_2S = 1:6:4) in acid medium (*p*H 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

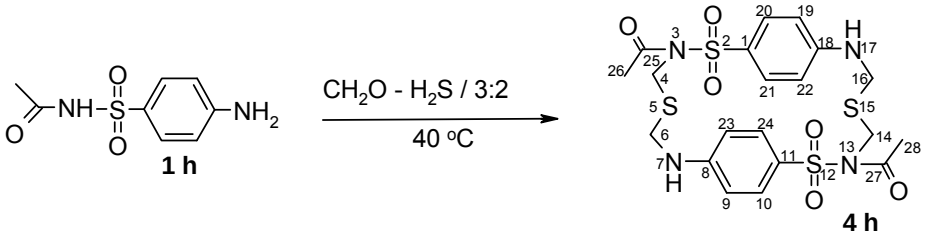
Reagent ratio **1g**:CH_2O:H_2S	*p*H	T, ºC	Yield (%)		
			2g	**4g**	**5g**
1 : 3 : 2	7.3-7.4	0	35	-	-
	7.3-7.4	20	58	-	-
	7.3-7.4	40	73	-	-
	7.3-7.4	80	52	14	-
1 : 6 : 4	1.3-1.5	40	-	-	93

The ^{1}H NMR spectrum of heterocycle **2g** exhibits proton signals of aromatic ring at δ_H 6.80-7.67 ppm. Singlet signals at δ_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 ^{13}C NMR spectrum for **2g** contains signals of the carbon atoms in aromatic rings at δ_C 116.48, 127.12, 133.99, and 147.86 ppm. The signals at δ_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 δ_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 δ_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 δ_C 112.73, 127.35, 131.91, and 149.39 ppm. The presence of signals at δ_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 δ_H 6.73-8.02, the methylene protons of SCH_2S and SCH_2N groups of the dithiazinane ring, linked with aromatic ring, are observed at δ_H 3.93 and 4.72 ppm (1:2 ratio), and of sulfo group at δ_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 δ_C 31.48 and 56.05 ppm, and with sulfo group at δ_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_2O-H_2S (Scheme 5) with 70% conversion. In neutral and alkaline medium, *p*-aniline sulfacetamide **1h** did not react with CH_2O and H_2S and 1,2,4-trithiolane was predominantly formed.[8]



Scheme 4. Cyclothiomethylation of *p*-aniline sulfo acetamide

The molecular weight of 543.53±10 (calc. M_{cr} 544) determined by Rast cryoscopy method[7] and the data of element analysis correspond to molecular formula $C_{20}H_{24}N_4O_6S_4$ that proved the formation of macroheterocycle **4h**. The ^{1}H NMR spectrum shows signals of methylene sulfide protons connected with amino group at δ_H 4.50 ppm, and connected with the sulfo acetamide group at δ_H 5.11 ppm. The ^{13}C NMR spectrum contains signals at δ_C 43.61 and 44.28 ppm assigned to carbon atoms of CH_2NH and CH_2NSO 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_2O H H_2S. 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 CH_2O and H_2S 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 CH_2O-H_2S 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 (*p*H 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 (*p*H 2,5) leads to cyclodimer **4h** (50%) built from two fragments of *p*-aniline sulfacetamide linked by *sym* dimethyl sulfide chain (CH_2SCH_2).

EXPERIMENTAL

All solvents were freshly distilled. The ^{1}H NMR spectra of compounds **2a-g**, **3b,d,e** and **4g**, **5g** were measured on spectrometer "Tesla BS-487", ^{13}C NMR - on spectrometer Jeol FX 90Q (22.50 MHz), internal standard - Me_4Si. 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 termal parameters have been deposited at the Cambrigdge 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 Na_2S and HCI) was barbotaged to give CH_2O–H_2S mixture at a ratio of 3:2 or 6:4. Then calculated amount of anylines (**la**, **1b**, **1c, 1d**, **le**, **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 C_6H_6/EtOAc (10:1) as the eluent. The products **2a–d, 3b**, **3d**, **2g**, **4g** were selected by fractional crystallization from $CHCl_3$. 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). ^{1}H NMR (80 MHz, DMSO-d_6): 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). ^{13}C NMR (22.5 MHz, DMSO-d_6): 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 $C_{10}H_{11}O_2NS_2$: 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). ^{1}H NMR (80 MHz, DMSO-d_6): 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). ^{13}C NMR (22.5 MHz, DMSO-d_6): 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 $C_{10}H_{11}O_2NS_2$: C 49.79, H 4. 56, N 5.80, S 26.55. Found: C 49.79, H 4.56, N 5.80, 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); 92 (48); 61 (100). ^{1}H NMR (80 MHz, DMSO-d_6): δ (ppm) 4.36 (br. s, 4 H, 2H-2, 2H-4), 6.72 (d, *J*=8.0 Hz, 2 H, H-6, H-10), 7.17 (d, *J*=8.0 Hz, 2 H, H-7, H-9), 7.75 (s, H, H-11). ^{13}C NMR (22.5 MHz, DMSO-d_6): 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 $C_9H_9O_2NS$: 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. ^{1}H NMR (80 MHz, DMSO-d_6): δ (ppm) 4.06 (s, 2 H, 2H-2), 5.20 (s, 4 H, 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, 2 H, H-13, H-14). ^{13}C NMR (22.5 MHz, DMSO-d_6): 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, 2900, 3360 cm^{-1}. *Anal*. Calcd for $C_{10}H_{11}O_3NS_2$: C 46.69, H 4.28, 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. ^{1}H NMR (80 MHz, DMSO-d_6): δ (ppm) 4.00 (s, 2 H, 2H-2), 5.20 (s, 4 H, 2H-4 and 2H-6), 6.80-7.50 (m, 3 H, H-8, H-11 and H-12), 8.45 (br. s, 2 H, H-13, H-14). ^{13}C NMR (22.5 MHz, DMSO-d_6): 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 $C_{10}H_{11}O_3NS_2$: C 46.69, H 4.28, 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. ^{1}H NMR (80 MHz, DMSO-d_6): 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). ^{13}C NMR (22.5 MHz, DMSO-d_6): 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 $C_9H_9O_3NS$: 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). ^{1}H NMR (80 MHz, $CDCl_3$): δ (ppm) 1.38 (t, *J*=7.2 Hz, 3 H, H_3C-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). ^{13}C NMR (22.5 MHz, $CDCl_3$): 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 $C_{12}H_{15}O_2NS_2$: 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). ^{1}H NMR (80 MHz, $CDCl_3$): δ (ppm) 1.34 (t, *J*=7.2 Hz, 3H, H_3C-14), 4.25 (k, *J*= 9.0 Hz, 2 H, H_2C-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). ^{13}C NMR (22.5 MHz, $CDCl_3$): 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 $C_{11}H_{13}O_2NS$: 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**:CH_2O:H_2S = 2:3:1 (yield 93%). White powder, mp 184-186 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.32 (t, *J*=6.5 Hz, 6 H, H_3C-22, H_3C-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). ^{13}C NMR (100 MHz, $CDCl_3$): 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 $C_{11}H_{13}O_2NS$: 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. ^{1}H NMR (80 MHz, $CDCl_3$): δ (ppm) 0.45 (t, *J*=6.3 Hz, 6 H, H_3C-19, H_3C-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). ^{13}C NMR (22.5 MHz, $CDCl_3$): 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, H 8.24, N 8.24, S 18.82. Found: C 51.97, H 7.46, N 7.70, S 19.50.

4-(1,3,5-Dithiazinane-5-yl)benzenesulfonamid (2g). White powder (73%). mp 135-137 ºC. ^{1}H NMR (80 MHz, DMSO-d_6): δ (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). ^{13}C NMR (22.5 MHz, DMSO-d_6): δ (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 $C_9H_{12}N_2S_3O_2$: C 39.11, H 4.38, N 10.14, S 34.80. Found: C 39.47, H 4.84, N 11.84, S 35.67.

2,2,12,12-Tetraon-2λ^6,5,12λ^6,15-tetrathia-3,7,13,17-tetraazatricyclo[16.2.2.2^{8,11}]-tetracosa-1(20),8,10, 18,21,23-hexaene (4g). White powder (14%). mp 146-148 ºC. ^{1}H NMR (80 MHz, DMSO-d_6): δ (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). ^{13}C NMR (22.5 MHz, DMSO-d_6): δ (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 $C_{16}H_{20}N_4S_4O_4$: C 41.72, H 4.38, N 12.16, S 27.85. Found: C 39.35, H 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 ºC. ^{1}H NMR (80 MHz, DMSO-d_6): δ (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, 2 H, H-8, H-12), 8.02 (d, *J*=7.98, 2 H, H-9, H-11). ^{13}C NMR (22.5 MHz, DMSO-d_6): δ (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, 1090, 1140, 1300, 1445, 1595, 2900 cm^{-1}. *Anal.* Calcd for $C_{12}H_{16}N_2S_5O_2$: C 37.87, H 4.24, N 7.36, S 42.13. Found: C 37.71, H 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}.

2,2,12,12-Tetraon-2λ^6,5,12λ^6,15-tetrathia-(3,13-diacyl)-3,7,13,17-tetraasatricyclo[16.2.2.2^{8,11}]-

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. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 1.88 (s, 6 H, H_3C-26, H_3C-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, NH-7, NH-17). ^{13}C NMR (100 MHz, DMSO-d_6): 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}. *Anal*. Calcd for $C_{20}H_{24}N_4S_4O_6$: C 44.10, H 4.48, N 10.09, S 23.55. Found: C 42.78, H 5.07, N 9.88, S 23.65.

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