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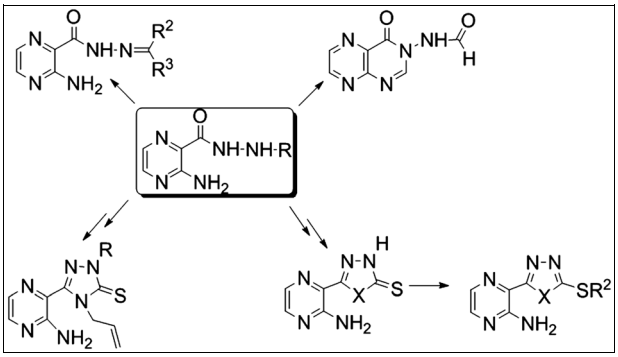

In research of new biologically active compounds, the reactions of amino-pyrazin-2-hydrazide and methylhydrazide with isothiocyanates, aromatic aldehydes, ketones, CS_2, and formic acid were made. New thiosemicarbazides, 1,3,4-thiadiazoles, 1,3,4-oxadiazoles, and 1,2,4-triazoles were obtained. New 4-oxopteridine derivative **26** was also synthesized.

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INTRODUCTION

Nitrogen heterocyclic compounds exhibit multidirectional pharmacological activity like diuretic [1,2], antitumor [3–6], and hypotensic [7–9]. 1,2,4-Triazole [10–12], 1,3,4-oxadiazole and 1,3,4-oxadiazole-2-thiones [6], quinazolones [13], pyrido[2,3-*d*]pyrimidines [1,2,14,15], and pteridine [5,16–19] belong to the most active group. Searching of the prospective biologically active compound we had interested in 3-amino-pyrazin-2-hydrazide analogs. The pyrazine derivatives are also used in many pharmaceuticals and plant protection products [20,21]. Our research concerns especially on compounds with potential tuberculostatic activity. Pyrazine derivatives like pyrazinamide are well known as therapeutics effective in infections cased by *M. tuberculosis*. Therefore, we have taken the synthesis of series of 3-amino-pyrazine derivatives bearing another heterocyclic system in C-2 position. Now, we report on the reactions of 3-amino-pyrazin-2-carbohydrazide **1** and its *N*′-methyl derivative **2**.

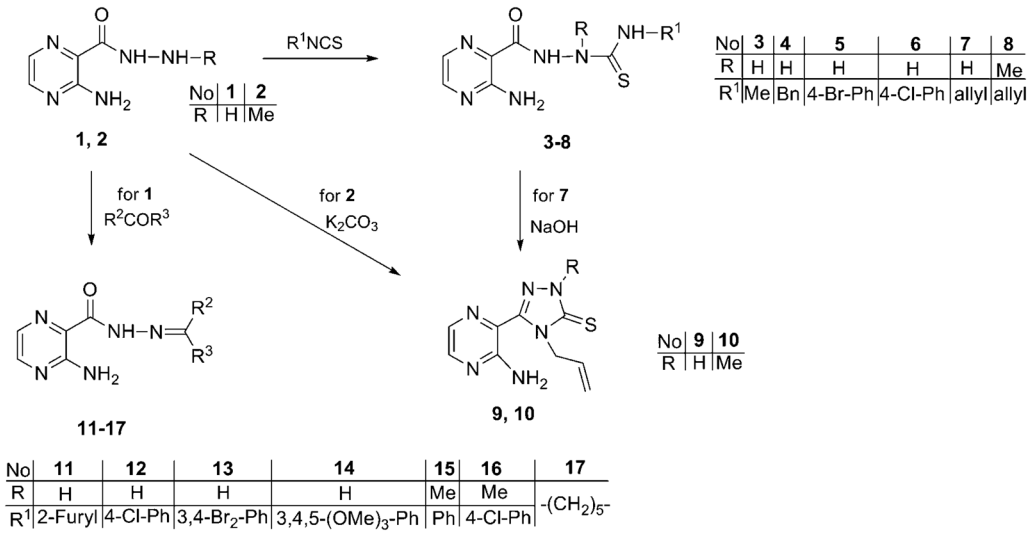
RESULTS AND DISCUSSION

The starting 3-amino-pyrazine-2-carbohydrazide **1** and 3-amino-*N*′-methylpyrazine-2-carbohydrazide **2** were obtained from methyl 3-amino-pyrazine-2-carboxylate in reaction with hydrazine hydrate or methylhydrazine (Scheme 1). Carbohydrazides **1** and **2** under treatment of appropriate isothiocyanates gave thiosemicarbazides **3**–**8**. Compound **7** heated in NaOH aqueous solution transformed to 1,2,4-triazole-3-thione **9**. In turn, its methyl analog derivative **10** was obtained directly from methylhydrazide **2** in K_2CO_3 aqueous solution and in the presence of allyl isothiocyanate. Analogical reaction with ethyl isothiocyanate in the presence of K_2CO_3 was performed by Shutske [10].

The condensation reaction of hydrazide **1** with aromatic aldehydes in EtOH in the presence of piperidine resulted formation of hydrazones **11**–**14**. Condensations with ketones were performed in dioxane with double excess of ketone or by refluxing reactants without solvent giving products **15**–**17**.

Reactions of carbohydrazide **1** with CS_2 led to 1,3,4-thiadiazole-2-thione **18** or 1,3,4-oxadiazole-2-thione **21** according to reaction conditions (Scheme 2). Compound **18** was synthesized from hydrazide **1** through the stage of potassium salt of 2-(3-amino-pyrazine-2-carbonyl)hydrazinecarbodithioic acid, which in concentrated H_2SO_4 underwent cyclization to 1,3,4-triazole-2-thione. Derivative **21** was obtained in a result of the reaction between hydrazide **1** and CS_2 in a presence of 1,8-diazabicyclo[5.4.0] undec-7-ene (DBU) as cyclization agent. However, in earlier reports, in reaction of CS_2 with antranile hydrazide or 2-aminonicotinic hydrazide, 3-amino-2- thioxo-quinazolin-4(3*H*)-one and 2-thioxo-1,3,4-benzotriazepin-5-one were got mainly [7,8,22]. In analogical reaction of 2-picolinhydrazide with CS_2 in alcohol, Liszkiewicz *et al.* [6] obtained 1,3,4-oxadiazole-2-thione.

Scheme 1



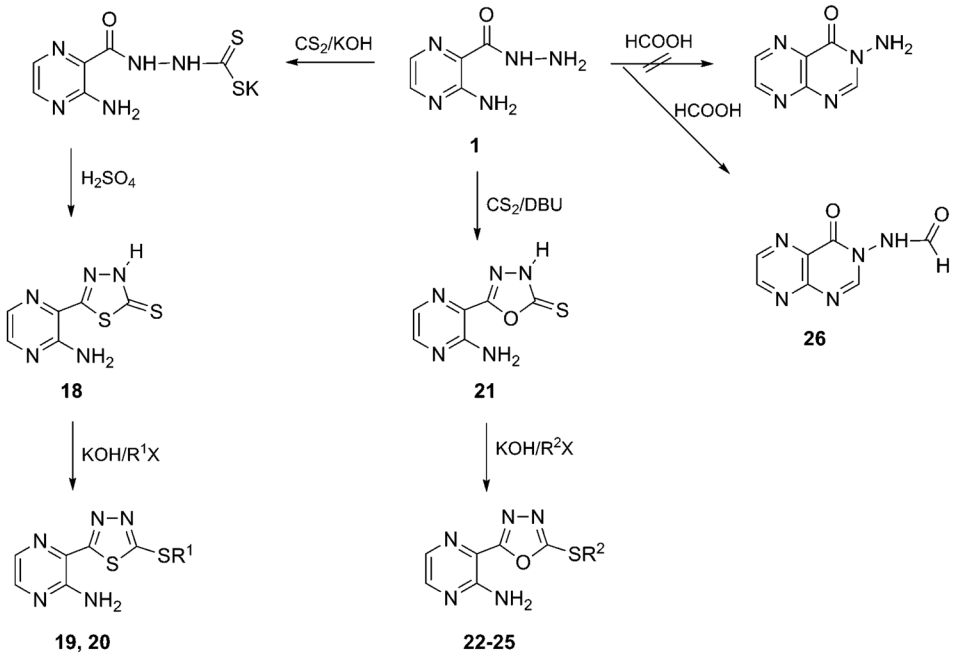
No	1	2
R	H	Me

No	3	4	5	6	7	8
R	H	H	H	H	H	Me
R^1	Me	Bn	4-Br-Ph	4-Cl-Ph	allyl	allyl

No	9	10
R	H	Me

No	11	12	13	14	15	16	17
R	H	H	H	H	Me	Me	$-(CH_2)_5-$
R^1	2-Furyl	4-Cl-Ph	3,4-Br_2-Ph	3,4,5-$(OMe)_3$-Ph	Ph	4-Cl-Ph	

Scheme 2



No	19	20
R^1	Me	CH_2COOEt

No	22	23	24	25
R^2	Me	CH_2COOEt	$(CH_2)_2NEt_2$	Ph-N⟨⟩N-$COCH_2$

1,3,4-Thiadiazole-2-thione **18** and 1,3,4-oxadiazole-2-thione **21** were undergone an alkylation to appropriate sulfides with methyl iodide (**19** and **22**) and ethyl bromoacetate (**20** and **23**) in ethanol–water solution of KOH. For 1,3,4-oxadiazole-2-thione **21**, reactions with *N*,*N*-diethylchloroethyleneamine hydrochloride and 2-chloro-1-(4-phenylpiperazin-1-yl)ethanone were also performed, and sulfides **24** and **25** were obtained.

In reaction of carbohydrazide **1** with formic acid, we expected to obtain 3-aminopteridin-4-(3*H*)-one according to reaction performed for 2-aminobenzamide by Reddy and coworkers [23]. However, we received formamide derivative **26**. Reaction details and physical constants of newly synthesized compounds are given in Table 1.

EXPERIMENTAL

All materials and solvents were of analytical reagent grade. Thin-layer chromatography was performed on Merck silica gel

Table 1

Characteristics of newly synthesized compounds **1**–**29**.

		m.p. (°C)	Formula	Calcd/found					
No	Yield (%)	Solvent	MW	C		H		N	
1	92	210–214	$C_5H_7N_5O$	39.21	39.18	4.61	4.60	45.73	45.81
		MeOH	153.14						
2	82	107–108	$C_6H_9N_5O$	43.11	43.09	5.43	5.41	41.89	41.90
		MeOH	167.17						
3	89	252–256	$C_7H_{10}N_6OS$	37.16	37.21	4.45	4.41	37.14	37.15
		DMF + H_2O	226.26						
4	60	204–207	$C_{13}H_{14}N_6OS$	51.64	51.61	4.67	4.66	27.80	27.79
		Dioxane + H_2O	302.35						
5	44	193–196	$C_{12}H_{11}BrN_6OS$	39.25	39.19	3.02	3.02	22.89	22.90
		Dioxane	367.22						
6	78	237–243	$C_{12}H_{11}ClN_6OS$	44.65	44.71	3.44	3.44	26.04	26.03
		DMF + H_2O	322.77						
7	87	187–189	$C_9H_{12}N_6OS$	42.85	42.83	4.79	4.80	33.31	33.32
		MeOH	252.30						
8	30	140–141	$C_{10}H_{14}N_6OS$	45.10	45.08	5.30	5.28	31.56	31.56
		Metanol	266.32						
9	72	299–301	$C_9H_{10}N_6S$	46.14	46.17	4.30	4.29	35.87	35.85
		DMF + MeOH	234.28						
10	40	139–140	$C_{10}H_{12}N_6S$	48.37	48.39	4.87	4.87	33.85	33.87
		MeOH	248.31						
11	70	186–189	$C_{10}H_9N_5O_2$	51.95	51.91	3.92	3.92	30.29	30.30
		MeOH + H	231.21						
12	88	259–262	$C_{12}H_{10}ClN_5O$	52.28	52.24	3.66	3.66	25.40	25.40
		Dioxane + H_2O	275.69						
13	77	246–249	$C_{12}H_9Cl_2N_5O$	46.47	46.51	2.92	2.92	22.58	22.59
		Dioxane + H_2O	310.14						
14	59	229–232	$C_{15}H_{17}N_5O_4$	54.38	54.40	5.17	5.15	21.14	21.15
		Dioxane	331.33						
15	88	230–232	$C_{13}H_{13}N_5O$	61.17	61.22	5.13	5.11	27.43	27.43
		Dioxane + MeOH	255.28						
16	56	247–249	$C_{13}H_{12}ClN_5O$	53.89	53.87	4.17	4.16	24.17	24.16
		Dioxane	289.72						
17	53	133–134	$C_{11}H_{15}N_5O$	56.64	56.66	6.48	6.46	30.02	30.03
		Dioxane + cyclohexane	233.27						
18	57	198–199	$C_6H_5N_5S_2$	34.11	34.13	2.39	2.39	33.15	33.15
		DMF + MeOH	211.27						
19	34	180–181	$C_7H_7N_5S_2$ 225.29	37.32	37.28	3.13	3.13	31.09	31.10
		MeOH							
20	30	258–260	$C_{10}H_{11}N_5O_2S_2$	40.39	40.35	3.73	3.73	23.55	23.54
		DMF + MeOH	297.36						
21	83	268–272	$C_6H_5N_5OS$	36.92	36.88	2.58	2.58	35.88	35.89
		DMF + MeOH	195.20						
22	73	192–193	$C_7H_7N_5OS$	40.18	40.22	3.37	3.37	33.47	33.47
		MeOH	209.23						
23	77	127–129	$C_{10}H_{11}N_5O_3S$	42.70	42.75	3.94	3.94	24.90	24.91
		EtOH	294.38						
24	58	164–165	$C_{12}H_{18}N_6OS$	48.96	48.89	6.16	6.14	28.55	28.54
		MeOH	294.38						
25	39	227–229	$C_{18}H_{19}N_7O_2S$	54.39	54.41	4.82	4.83	24.67	26.67
		DMF + MeOH	397.45						
26	62	213–214	$C_7H_5N_5O_2$	43.98	43.92	2.64	2.64	36.64	36.61
		EtOH + H_2O	191.15						

$60F_{254}$ plates and visualized with UV. The results of elemental analyses (%C, H, N) for all of obtained compounds were in agreement with calculated values within ±0.3% range. ^{1}H-NMR spectra in $CDCl_3$ or DMSO-d_6 were recorded on Varian Unity Plus (500 MHz) and Varian Gemini (200 MHz) instruments. IR Spectra (KBr) were determined as KBr pellets of the solids on a Satellite FT-IR spectrophotometer. Mass spectra for compounds **11**, **18**, **19**, **21**, **22**, and **26** were taken on Biosystem Qstar XL MS/MS spectrometer with electro spray ionization system (70 eV). Melting points were determined on BOETIUS apparatus and were uncorrected.

3-Amino-pyrazine-2-carbohydrazide (1). The suspension of 4.6 g (30 mmol) of methyl 3-amino- pyrazine-2-carboxylate and 3 mL (60 mmol) of 98% hydrazine hydrate in 30 mL of EtOH was refluxed for 4 h. Then, the mixture was cooled, and the product was filtered and recrystallized from MeOH. Yield 92%; m.p. 211–213°C. (lit. ref. [19], m.p. 210–211°C).

3-Amino-*N*′-methylpyrazine-2-carbohydrazide (2). To the solution of 4.6 g (30 mmol) of methyl 3-amino-pyrazine-2-carboxylate in 10 mL of EtOH and 20 mL of dioxane, 3.2 mL (80 mmol) of methylhydrazine was added. The mixture was refluxed for 4 h. Then, the solvent was evaporated, and the residue was treated with 2 mL of MeOH and 5 mL of diethyl ether. The precipitate was filtered and recrystallized from MeOH. Yield 82%; m.p. 107–108°C. (lit. ref. [10], m.p. 105–107°C).

General procedure for the synthesis of 2-(3-amino-pyrazine-2-carbonyl)hydrazinecarbothioamides (3–7). Carbohydrazide **1** (0.38 g, 2.5 mmol) was dissolved in 15 mL of anhydrous dioxane, and 2.5 mmol of suitable isothiocyanate was added. The mixture was refluxed for 4–8 h. Reaction progress was controlled with TLC method. Then, the solvent was evaporated, and the residue was treated with toluene. The crude solid was filtered and recrystallized.

2-(3-Amino-pyrazine-2-carbonyl)-N-methylhydrazine-carbothioamide (3). This compound was obtained as colorless small needles. IR: 3359 (ν N—H), 3307 (ν N—H), 3210 (ν N—H), 2933 (ν C—H), 1655 (ν C═O), 1625 (ν C═N), 1556 (δ N—H), 1491 (δ N—H), 1070 (ν C═S), 926 (γ C—H), 760 (γ N—H) cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d_6): δ 2.82 (d; 3H, CH_3, *J* 4.4 Hz), 7.40 (brs; 2H, NH_2 + D_2O [-]), 7.80 (d; 1H, pyrazine, *J* 2.3 Hz), 7.93–7.96 (m; 1H, NH + D_2O exchangeable), 8.24 (d; 1H, pyrazine, *J* 2.3 Hz), 9.20 (brs; 1H, NH + D_2O exchangeable), 10.40 (brs; 1H, NH + D_2O exchangeable) ppm.

2-(3-Amino-pyrazine-2-carbonyl)-N-benzylhydrazinecarbothiamide (4). This compound was obtained as light beige prisms. IR: 3270 (ν N—H), 3180 (ν N—H), 2957 (ν C—H), 2851 (ν C—H), 1680 (ν C═O), 1602 (ν C═N), 1552 (δ N—H), 1046 (ν C═S), 871 (γ C—H), 815 (γ C—H), 742 (γ N—H) cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d_6): δ 4.70 (d; 2H,CH_2, *J* 6.14), 7.26–7.29 (m; 5H, Ph), 7.44 (brs; 2H, NH_2), 7.80 (d; 1H, pyrazine, *J* 2.3 Hz), 8.20 (d; 1H, pyrazine, *J* 2.4 Hz), 8.54 (brs; 1H, N*H*CH_2), 9.40 (s; 1H, NH), 10.53 (s; 1H, NH) ppm.

2-(3-Amino-pyrazine-2-carbonyl)-N-(4-bromophenyl) hydrazinecarbothioamide (5). This compound was obtained as white prisms. IR: 3373 (ν N—H), 3273 (ν N—H), 3198 (ν N—H), 2957 (ν C—H), 2913 (ν C—H), 1675 (ν C═O), 1624 (ν C═N), 1530 (δ N—H), 1045 (ν C═S), 870 (γ C—H), 727 (γ N—H) cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d_6): δ 7.46–7.48 (m; 6H, 4H Ph and 2H NH_2), 7.85 (d; 1H, pyrazine, *J* 2.4 Hz), 8.25 (d; 1H, pyrazine, *J* 2.4 Hz), 8.58 (s; 1H, NH), 9.75 (brs; 1H, NH), 10.62 (s; 1H, NH) ppm.

2-(3-Amino-pyrazine-2-carbonyl)-N-(4-chlorophenyl) hydrazinecarbothioamide (6). This compound was obtained as small prisms. IR: 3374 (ν N—H), 3289 (ν N—H), 3171 (ν N—H), 3100 (ν N—H), 2912 (ν C—H), 1678 (ν C═O), 1627 (ν C═N), 1561 (δ N—H), 1525 (δ N—H), 1060 (ν C═S), 889 (γ C—H), 848 (γ C—H), 789 (γ N—H) cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d_6): δ 7.30–7.50 (m; 6H, 4H Ph, and 2H NH_2), 7.86 (d; 1H, pyrazine, *J* 2.3 Hz), 8.24 (d; 1H, pyrazine, *J* 2.3 Hz), 8.62 (s; 1H, NH), 9.75 (s; 1H, NH), 10.62 (s; 1H, NH) ppm.

N-Allyl-2-(amino-pyrazine-2-carbonyl)hydrazinecarbothioamide (7). This compound was obtained as colorless crystals. IR: 3310 (ν N—H), 3100 (ν N—H), 2979 (ν C—H), 2900 (ν C—H), 1680 (ν C═O), 1614 (ν C═N), 1546 (δ N—H), 1062 (ν C═S), 927 (γ C—H), 860 (γ C—H) cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d_6): δ 4.05–4.09 (m; 2H, CH_2), 5.08 (dd; 2H, CH_2, *J* 1.8 Hz), 5.80–5.83 (m; 1H, CH), 7.45 (brs; 2H, NH_2), 7.84 (d, 1H, pyrazine, *J* 2.3 Hz), 8.15–8.19 (m; 1H, N*H*CH_2), 8.22 (d; 1H, pyrazine, *J* 2.3 Hz), 9.31 (s; 1H, NH), 10.45 (s; 1H, NH) ppm.

***N*-Allyl-2-(amino-pyrazine-2-carbonyl)-1-methylhydrazine-carbothioamide (8).** To 0.25 g (1.5 mmol) of methylhydrazide **2** dissolved in 15 mL of dioxane 0.15 mL (1.5 mmol) of allyl isothiocyanate was added. The mixture was refluxed for 1.5 h and cooled down. Then, solvent was evaporated, and 15 mL of diethyl ether was added to the residue. Crude product was filtered and recrystallized. IR: 3410 (ν N—H), 3270 (ν N—H), 1679 (ν C═O), 1604 (ν C═N), 1528 (δ N—H), 1480 (δ N—H), 1050 (ν C═S), 923 (γ C—H), 812 (γ C—H) cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.69 (s; 3H, CH_3), 4.27–4.31 (m; 2H, CH_2), 5.13–5.16 (m; 2H, CH_2), 5.84–5.88 (m; 1H, CH), 6.58 (brs; 2H, NH_2), 7.84 (d; 1H, pyrazine, *J* 2.0 Hz), 8.22 (d; 1H, pyrazine, *J* 2.0 Hz), 9.40 (s; 1H, NH) ppm.

4-Allyl-3-(3-amino-pyrazin-2-yl)-1*H*-1,2,4-triazole-5 (4*H*)-thione (9). Compound **7** (1.26 g, 5 mmol) was refluxed for 2 h in 20 mL of 10% NaOH aqueous solution. The mixture was cooled and acidified with acetic acid. The precipitate was filtered and recrystallized. IR: 3386 (ν N—H), 3162 (ν N—H), 1621 (ν C═N), 1555 (δ N—H), 1469 (δ N—H), 984 (γ C—H), 835 (γ C—H) cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6): δ 4.95 (d; 1H, CH, *J* 17,1 Hz), 5.06 (d; 1H, CH, *J* 10.3 Hz), 5.15 (d; 2H, *J* 4.9 Hz), 5.84–5.22 (m; 1H, CH), 7.20 (s; 2H, NH_2), 7.94 (d; 1H, pyrazine, *J* 2.0 Hz), 14.28 (s; 1H, NHCS) ppm.

4-Allyl-3-(3-amino-pyrazin-2-yl)-1-methyl-1,2,4-triazole-5 (4*H*)-thione (10). Methylhydrazide **2** (0.25 g, 1.5 mmol) was dissolved in 5 mL of 10 % K_2CO_3. Then, 1.5 mL (15 mmol) of allyl isothiocyanate and 2 mL of dioxane were added. The mixture was refluxed for 1.5 h, cooled and 10 mL of water was added. The crude product was filtered and recrystallized yielding bright needles. IR: 3389 (ν N—H), 3128 (ν N—H), 1625 (ν C═N), 1469 (δ N—H), 925 (γ C—H) cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.95 (s; 3H, CH_3), 5.20 (m; 2H, CH_2), 5.44 (d; 2H, CH_2, *J* 5.9 Hz), 5.96 (m; 1H, CH), 6.60 (brs; 2H, NH_2), 8.02 (d; 1H, pyrazine, *J* 2.4 Hz), 8.09 (d, 1H, pyrazine, *J* 2.4 Hz) ppm.

General procedure for the synthesis of 3-amino-*N*′-methylenepyrazine-2-carbohydrazide derivatives (11–14). Hydrazide **1** (0.25 g, 1.6 mmol) was dissolved in 10 mL of anhydrous ethanol and equimolar amount of suitable aldehyde and four drops of piper dine were added. The mixture was refluxed for 4–8 h. The reaction progress was observed with TLC method. Then the solvent was evaporated to 1/3 of the volume. The solution was cooled, and the given precipitate was filtered and recrystallized.

3-Amino-N*′*-(furan-2-ylmethylene)pyrazine-2-carbohydrazide (11). This compound was obtained as white powder. IR: 3289 (ν N—H), 3230 (ν N—H), 3142 (ν N—H), 1680 (ν C═O), 1644 (ν C═N), 1598 (δ N—H), 1519 (δ N—H), 1160 (ν C—O), 946 (γ C—H), 858 (γ C—H), 749 (γ N—H) cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6): δ 6.63 (t, 1H, furan, *J* 3.4 Hz) 6.88 (d; 1H, furan, *J* 3.3 Hz), 7.60 (brs; 2H, NH_2), 7.84 (d; 1H furan, *J* 1.8 Hz), 7.88 (d; 1H, pyrazine, *J* 2.3 Hz), 8.27 (d; 1H,

pyrazine, *J* 2.4 Hz), 8.48 (s; 1H, CH), 12.08 (s; 1H, NHCO + D_2O exchangeable) ppm; MS: *m*/*z* 231 (M^+).

3-Amino-N′-(4-chlorobenzylidene)pyrazine-2-carbohydrazide (12). This compound was obtained as white powder. IR: 3317 (ν N—H), 3256 (ν N—H), 3148 (ν N—H), 1674 (ν C=O), 1612 (ν C=N), 1593 (δ N—H), 1513 (δ N—H), 866 (γ C—H), 733 (γ N—H), 700 (ν C—Cl) cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d_6): δ 7.52 (d; 2H, Ph, *J* 8.5 Hz), 7.60 (brs; 2H, NH_2), 7.70 (d; 2H, Ph, *J* 8.6 Hz), 7.89 (d; 1H, pyrazine, *J* 2.4 Hz), 8.27 (d; 1H, pyrazine, *J* 2.3 Hz), 8.58 (s; 1H, CH), 12.10 (s; 1H, NHCO) ppm.

3-Amino-N′-(3,4-chlorobenzylidene)pyrazine-2-carbohydrazide (13). This compound was obtained as white powder. IR: 3385 (ν N—H), 3250 (ν N—H), 3148 (ν N—H), 2962 (ν C—H), 1672 (ν C=O), 1612 (ν C=N), 1530 (δ N—H), 881 (γ C—H), 836 (γ C—H) cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d_6): δ 7.60 (brs; 2H, NH_2), 7.66–7.70 (m; 2H, Ph), 7.85 (s; 1H, Ph), 7.88 (d; 1H, pyrazine, *J* 2.3 Hz), 8.27 (d; 1H, pyrazine, *J* 2.3 Hz), 8.55 (s; 1H, CH), 12.20 (s; 1H, NHCO) ppm.

3-Amino-N′-(3,4,5-trimethoxybenzylidene)pyrazine-2-carbohydrazide (14). This compound was obtained as white powder. IR: 3438 (ν N—H), 3260 (ν N—H), 3103 (ν N—H), 2936 (ν C—H), 2842 (ν C—H), 1672 (ν C=O), 1612 (ν C=N), 1577 (δ N—H), 1527 (δ N—H), 1166 (ν C—O), 925 (γ C—H), 853 (γ C—H) cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d_6): δ 3.69 (s; 3H, CH_3), 3.83 (s, 6H, $2CH_3$), 6.97 (s; 2H, Ph), 7.60 (s; 2H, NH_2), 7.88 (d; 1H, pyrazine, *J* 2.4 Hz), 8.27 (d; 1H, *J* 2.4 Hz) 8.49 (s; 1H, CH), 12.00 (s; 1H, NHCO + D_2O exchangeable) ppm.

General procedure for the synthesis of 3-amino-*N*′-methylenepyrazine-2-carbohydrazide derivatives (15–17). To 0.25 g (1.6 mmol) of hydrazide **1** in 15 mL of dioxane double excess (3.2 mmol) of suitable ketone was added. The mixture was refluxed for 12–24 h. Then mixture was concentrated to 1/3 of its volume and cooled. The precipitate was filtered and recrystallized. Compound **16** was obtained from hydrazide **1** (1.6 mmol) by refluxing in 6 mL of cyclohexanone. After concentration 10 mL of toluene was added. The solid was filtered and recrystallized.

3-Amino-N′-(1-phenylethylidene)pyrazine-2-carbohydrazide (15). This compound was obtained as white powder. IR: 3336 (ν N—H), 3247 (ν N—H), 3142 (ν N—H), 1677 (ν C=O), 1606 (ν C=N), 1560 (δ N—H), 1511 (δ N—H), 857 (γ C—H), 810 (γ C—H) cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.40 (s; 3H, CH_3), 7.28 (brs; 2H, NH_2), 7.38–7.41 (m; 3H, Ph), 7.84 (d; 1H, pyrazine, *J* 2.4 Hz), 7.84–7.89 (m; 2H, Ph), 8.20 (d; 1H, pyrazine, *J* 2.4 Hz), 10.78 (s; 1H, NHCO) ppm.

3-Amino-N′-(1-(4-chlorophenyl)ethylidene)pyrazine-2-carbohydrazide (16). This compound was obtained as light beige powder. IR: 3396 (ν N—H), 3258 (ν N—H), 3147 (ν N—H), 1680 (ν C=O), 1613 (ν C=N), 1562 (δ N—H), 860 (γ C—H), 842 (γ C—H), 764 (γ N—H), 698 (ν C—Cl) cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.38 (s; 3H, CH_3), 7.18 (brs; 2H, NH_2), 7.34–7.38 (m; 2H, Ph), 7.80–7.86 (m; 3H, 2H Ph and 1H pyrazine), 8.22 (d; 1H, pyrazine, *J* 2.4 Hz), 10.80 (s; 1H, NHCO) ppm.

3-Amino-N′-cyclohexylidenepyrazine-2-carbohydrazide (17). This compound was obtained as small white crystals. IR: 3395 (ν N—H), 3264 (ν N—H), 3150 (ν N—H), 2937 (ν C—H), 2851 (ν C—H), 1680 (ν C=O), 1616 (ν C=N), 1502 (δ N—H), 935 (γ C—H), 856 (γ C—H) cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.70–1.80 (m; 6H, $2CH_3$), 2.40–2.43 (m; 4H, $2CH_2$), 7.05 (brs; 2H, NH_2), 7.78 (d; 1H, pyrazine, *J* 2.2 Hz), 8.17 (d; 1H, pyrazine, *J* 2.3 Hz), 10.56 (s; 1H, NHCO) ppm.

5-(3-Amino-pyrazin-2-yl)-1,3,4-thiadiazole-2(3*H*)-thione (18). To 1.53 g (10 mmol) of hydrazide **1**, the solution of 0.68 g (12 mmol) of KOH in 3 mL of water and 20 mL of ethanol was added. The mixture was refluxed for 2 h. Then, 30 mL of diethyl ether was added the precipitated salt, and solid was filtered. Yield 88%; m.p. 316–319°C.

The obtained potassium salt (2.65 g, 10 mmol) was heated in 20 mL of concentrated H_2SO_4 at 90°C for 1 h. Then, the mixture was poured onto 50 g of ice. The solid was filtered, dissolved in 30% NaOH aqueous solution, precipitated with acetic acid, and recrystallized. IR: 3421 (ν N—H), 3160 (ν N—H), 2853 (ν C—H), 1620 (ν C=N), 1560 (δ N—H), 1071 (ν C=S), 995 (γ C—H), 734 (γ N—H) cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d_6): δ 7.10 (brs; 2H, NH_2), 8.00 (d; 1H, pyrazine, *J* 2.3 Hz), 8.24 (d; 1H, pyrazine, *J* 2.3 Hz), 14.00 (s; 1H, NHCO) ppm; MS: *m*/*z* 211 (M^+).

General procedure for the synthesis of sulfide derivatives (19, 20). Compound **18** (2.5 mmol) was added to the solution of 0.2 g of KOH in 10 mL of water and 10 mL of ethanol. The mixture was stirred until dissolved. Then, 0.21 mL (3.3 mmol) of iodomethane or 0.28 mL (2.5 mmol) of ethyl bromoacetate was added and refluxed for 1 h. Then, mixture was cooled, and solid was filtered and recrystallized.

2-(3-Amino-pyrazin-2-yl)-5-methylthio-1,3,4-thiadiazole (19). This compound was obtained as white powder. IR: 3372 (ν N—H), 3153 (ν N—H), 1637 (ν C=N), 992 (γ C—H), 751 (γ N—H) cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.86 (s; 3H, CH_3), 7.15 (brs; 2H, NH_2), 7.99–8.04 (m; 2H, pyrazine) ppm; MS: *m*/*z* 225 (M^+).

Ethyl 2-(5-(3-amino-pyrazin-2-yl)-1,3,4-thiadiazol-2-ylthio) acetate (20). This compound was obtained as white powder. IR: 3384 (ν N—H), 3155 (ν N—H), 1733 (ν C=O), 1632 (ν C=N), 1558 (δ N—H), 1025 (ν C—O), 762 (γ N—H) cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.31 (t, 3H, CH_3, *J* 7 Hz), 4.20 (s; 2H, CH_2), 4.29 (q; 2H, CH_2, *J* 7.1 Hz), 7.17 (brs; 2H, NH_2), 7.95–8.05 (m; 2H, pyrazine) ppm.

5-(3-Amino-pyrazin-2-yl)-1,3,4-oxadiazole-2(3*H*)-thione (21). Hydrazide **1** (1.53 g, 10 mmol) was added to the solution of 1.5 mL (10 mmol) of DBU and 1 mL (10 mmol) of CS_2 in 50 mL of ethanol. The mixture was refluxed for 10 h. Then, the solvent was evaporated, and 20 g of ice was added to the residue. The mixture was acidified with acetic acid, solid was filtered and recrystallized. IR: 3373 (ν N—H), 3289 (ν N—H), 3171 (ν N—H), 2912 (ν C—H), 1627 (ν C=N), 1493 (δ N—H), 1088 (ν C=S), 949 (γ C—H) 788 (γ N—H) cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d_6): δ 7.17 (brs; 2H, NH_2), 7.99 (d; 1H, pyrazine, *J* 2.4 Hz), 8.24 (d; 1H, pyrazine, *J* 2.4 Hz) ppm; MS: *m*/*z* 195 (M^+).

General procedure for the synthesis of sulfides (22–25). Compound **21** (0.49 g, 2.5 mmol) was added to the solution of 0.2 g (3.5 mmol) of KOH in 10 mL of ethanol and 10 mL of water. The mixture was stirred until dissolved. Then, 3.3 mmol (0.21 mL) of iodomethane or 2.5 mmol of ethyl bromoacetate, *N*,*N*-diethylchloroethylenediamine hydrochloride or 2-chloro-1-(4-phenylpiperazin-1-yl)ethanone was added. The mixture was stirred at room temperature for 2 h. Then, solid was filtered and recrystallized.

2-(3-Amino-pyrazin-2-yl)-5-methylthio-1,3,4-oxadiazole (22). This compound was obtained as light beige needles. IR: 3293 (ν N—H), 3158 (ν N—H), 1637 (ν C=N), 1570 (δ N—H), 1477 (δ N—H), 1081 (ν C—O), 992 (γ C—H), 843 (γ C—H)

cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.82 (s; 3H, CH_3), 6.67 (brs; 2H, NH_2), 8.07 (d; 1H, pyrazine, *J* 2.4 Hz), 8.17 (d; 1H, pyrazine, *J* 2.4) ppm; MS: *m*/*z* 209 (M^+).

Ethyl 2-(5-(3-amino-pyrazin-2-yl)-1,3,4-oxadiazol-2-ylthio) acetate (23). This compound was obtained as light beige needles. IR: 3295 (ν N—H), 3143 (ν N—H), 2935 (ν C—H), 1742 (ν C═O), 1636 (ν C═N), 1475 (δ N—H), 1087 (ν C—O), 893 (γ C—H) cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d_6): δ 1.19 (t; 3H, CH_3, *J* 7.0 Hz), 4.17 (q; 2H, CH_2, *J* 7.1 Hz), 4.29 (s; 2H, CH_2), 7.46 (brs; 2H, NH_2), 8.00 (d; 1H, pyrazine, *J* 2.4 Hz), 8.25 (d; 1H, pyrazine, *J* 2.4 Hz) ppm.

2-(3-Amino-pyrazin-2-yl)-5-(2-(diethylamino)ethylthio)-1,3, 4-oxadiazole (24). This compound was obtained as small beige needles. IR: 3281 (ν N—H), 3148 (ν N—H), 2967 (ν C—H), 1625 (ν C═N), 1466 (δ N—H), 1085 (ν C—O), 849 (γ C—H), 757 (γ N—H) cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.12–1.18 (m; 6H, $2CH_3$), 2.73–2.82 (m; 4H, $2CH_2$), 3.01 (m; 2H, CH_2), 3.54–3.60 (m; 2H, SCH_2), 6.56 (brs; 2H, NH_2), 8.05 (d; 1H, pyrazine, *J* 2.4 Hz), 8.16 (d; 1H, pyrazine, *J* 2.4 Hz) ppm.

2-(5-(3-Amino-pyrazin-2-yl)-1,3,4-oxadiazol-2-ylthio)-1-(4-phenylpiperazin-1-yl)ethanone (25). This compound was obtained as small white needles. IR: 3287 (ν N—H), 3163 (ν N—H), 3053 (ν N—H), 2923 (ν C—H), 1669 (ν C═O), 1470 (δ N—H), 1085 (ν C—O), 930 (γ C—H), 763 (γ N—H) cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d_6): δ 3.18–3.22 (m; 4H, CH_2NCH_2), 3.62–3.67 (m; 4H, CH_2NCH_2), 4.63 (s; 2H, CH_2), 6.80 (t; 1H, Ph, *J* 7.3 Hz), 6.97 (d; 2H, Ph, *J* 7.6 Hz), 7.24 (t; 2H, Ph, *J* 7.4 Hz), 7.47 (brs; 2H, NH_2), 9.97 (d; 1H, pyrazine, *J* 2.3 Hz), 8.24 (d; 1H, pyrazine, *J* 2.2 Hz) ppm.

***N*-(4-Oxopteridin-3-(4*H*)-yl)formamide (26).** Hydrazide **1** (0.76 g (5 mmol) and 5 mL of formic acid were refluxed for 4 h. Then, mixture was cooled, and ammonium hydroxide was added. The solid precipitate was filtered and recrystallized. IR: 3298 (ν N—H), 2999 (ν C—H), 1687 (ν C═O), 1621 (ν C═N), 1461 (δ N—H), 933 (γ C—H), 737 (γ N—H), cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d_6): δ 7.47 (s; 1H, NH), 7.85 (d; 1H, pyrazine, *J* 2.1 Hz), 8.08 (s; 1H, CH), 8.26 (d; 1H, pyrazine, *J* 2.2 Hz), 8.39 (s; 1H, CHO) ppm; MS: *m*/*z* 191 (M^+).

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