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Environmentally Safe One-Pot Solvent-Free Synthesis of 6-Aryl-1,2,4,5-tetrazinane-3-thiones(ones) Catalyzed by $NaHSO_4$-SiO_2

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Abstract—One-pot condensation of thiourea (urea), diverse aromatic aldehydes, and ammonium acetate in the presence of repeatedly usable heterogeneous catalyst $NaHSO_4$–SiO_2 in the absence of solvent under the microwave irradiation proceeds faster and with better yields of 6-aryl-1,2,4,5-tetrazinane-3-thiones(ones) that under common heating. Compounds synthesized exist as a rule as two isomers distinguished by the position of the phenyl ring: It is located in the major isomer nearly in the equatorial position, in the minor one, close to axial position.

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The application of multi-component reactions (MCR) including domino processes [1] involving at least three various simple substrates [2] that react in a definite way to form a single product is a powerful synthetic strategy [3]. Since the first MCR [4] this well-known concept [5] widely spread also in the nature has been extensively employed both in the liquid-phase [3] and in solid-phase [6] chemistry for quick building of complex heterocyclic structures important for development of pharmacy [7].

Owing to the necessity of the "environmentally safe technological revolution" [8] a considerable attention is given to the procedure of microwave irradiation for ensuring fast synthesis of versatile organic compounds because of selective absorption of the microwave energy by polar molecules. The use of heterogeneous catalysts, in particular, $NaHSO_4$ on SiO_2 carrier [9], became a milestone in various fields of chemistry due to environmental safety combined with good yields and selectivity. Moreover, $NaHSO_4$–SiO_2 is a nontoxic and noncorrosive substance, and the possibility of repeated use of $NaHSO_4$–SiO_2 in certain processes actually results in more environmentally friendly synthetic procedures.

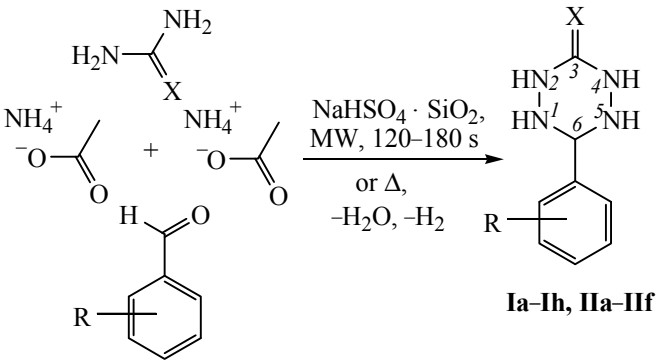
1,2,4,5-Tetrazines are an important class of heterocyclic compounds finding many practically useful synthetic applications [10]. Nowadays due to their efficiency in the cancer therapy the 1,2,4,5-tetrazines are investigated in the National Cancer Institute in USA [11]. These interesting results prompted us to investigate the reaction described further.

Inasmuch as the formation of an N–N bond is a relatively difficult process the 1,2,4,5-tetrazines are commonly obtained from hydrazine derivatives or from nitrile imines. A reaction was described of a number of monohydrazones of simple aliphatic aldehydes and ketones with thiocarbohydrazide and 6-alkylhexahydro-1,2,4,5-tetrazine-3-thiones [12].

In the present study 6-aryl-1,2,4,5-tetrazinane-3-thiones(ones) **Ia–Ih**, **IIa–IIf** were prepared by multicomponent cyclocondensation of 1 mol of thiourea (urea), 1 mol of substituted benzaldehyde, and 2 mol of ammonium acetate in the presence of hetero-geneous catalyst $NaHSO_4$–SiO_2 in the absence of solvent under the microwave irradiation or at common heating (Scheme 1).

The reaction was carried out at 80°C and the power of the microwave radiation of 320 W for 120–180 s or at heating on an oil bath for 30–70 min at 75°C. On the completion of the reaction (TLC monitoring) the reaction mixture was extracted with ethyl acetate, the extract was concentrated in a vacuum, the residue was purified by column chromatography using as eluent a mixture

Scheme 1.



Ia–Ih, IIa–IIf

I: X = S, R = H (**a**), 4-Cl (**b**), 2-Cl (**c**), 4-F (**d**), 4-Me (**e**), 4-MeO (**f**), 2-Me (**g**), 3-PhO (**h**); **II**, X = O, R = Ph (**a**), 4-Cl (**b**), 4-F (**c**), 4-Me (**d**), 4-MeO (**e**), 3-NO_2 (**f**).

benzene–ethyl acetate, 2:8. The stoichiometry of the reaction [the ratio thiourea (urea):NH_4OAc:benzaldehyde 1:2:1] also indicated the formation of new 6-aryl-1,2,4,5-tetrazinane-3-thiones(ones).

In order to detect the possible specific (not only thermal) effect of the microwave irradiation we also studied the reaction at an ordinary heating on an oil bath. Even at a long reaction time under the ordinary heating the yields were lower than at the microwave activation (Table 1).

These facts clearly show that the effect of the microwave irradiation is not purely thermal. This behavior is consistent with the assumed reaction mechanism [13] shown in Scheme 2. Inasmuch as the reaction proceeds in a polar environment the specific microwave effects

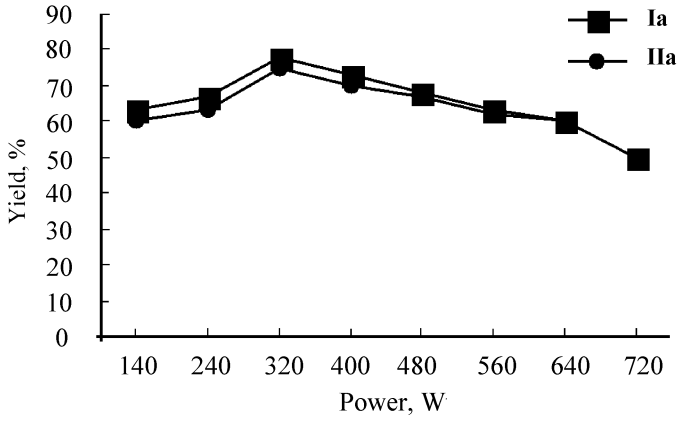


Fig. 1. Optimization of power level of microwave radiation in the synthesis of 6-aryl-1,2,4,5-tetrazinane-3-thiones(ones) **Ia** and **IIa**.

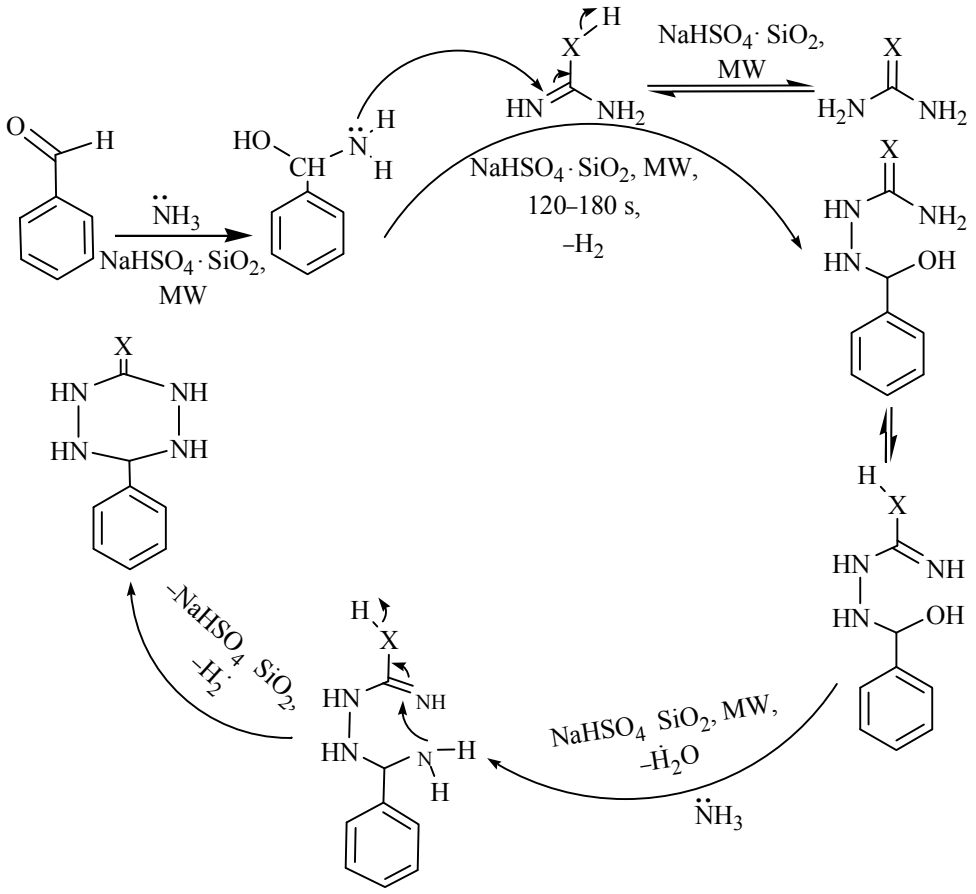
Table 1. Comparison of results of synthesis of 6-aryl-1,2,4,5-tetrazinane-3-thiones(ones) **Ia–Ih**, **IIa–IIf** under microwave irradiation (MW, 75–78°C) and at common heating (Δ, 75°C)

Compound no.	Method	Reaction time, s	Yield, %
Ia	MW	120	78
	Δ	120, 1800	20, 35
Ib	MW	160	76
	Δ	160, 2100	22, 30
Ic	MW	180	74
	Δ	2280	33
Id	MW	140	80
	Δ	1980	40
Ie	MW	150	75
	Δ	150, 2400	24, 35
If	MW	155	78
	Δ	2460	32
Ig	MW	160	74
	Δ	1980	35
Ih	MW	180	72
	Δ	2700	30
IIa	MW	130	75
	Δ	130, 2100	28, 38
IIb	MW	150	70
	Δ	2280	33
IIc	MW	165	68
	Δ	165, 2580	20, 30
IId	MW	140	70
	Δ	2400	35
IIe	MW	155	73
	Δ	2460	37
IIf	MW	180	70
	Δ	2580	30

can be revealed when the transition state is more polar that the initial state of the reaction. Since the dipole-dipole electrostatic interactions are more pronounced in the transition state, its stabilization is higher that that of the initial state resulting in the decrease in the activation energy. The polarity of the system in the transition state increases due to the formation of looser ion pairs that in the initial state (Scheme 2).

Further we carried out the synthesis of compounds **Ia** and **IIa** varying the power of the microwave radiation from 80 to 720 W in order to choose the most suitable power level. The results are shown on the plot in Fig. 1 indicating that the maximum yield is attained at the power of 320 W.

Scheme 2.



We tested the possibility of the repeated application of $NaHSO_4$–SiO_2. The results are shown in Fig. 2. The catalyst was easily regenerated by washing with ethyl acetate followed by drying at 110°C for 1 h. Therewith the catalytic activity was retained in the course of six runs. However the activity notably decreased after 4 runs due to the accumulation of organic substances. The organic substances adsorbed on the solid surface decreased the number of active sites. Also $NaHSO_4$ was partially washed out from the SiO_2 carrier. The organic substances can be removed at higher temperature for reactivation of the catalyst.

The composition and structure of 6-aryl-1,2,4,5-tetrazinane-3-thiones(ones) **Ia–Ih**, **IIa–IIf** were proved by elemental analysis, mass, IR, ^1H and ^{13}C NMR spectra and by 2D NMR spectroscopy with the use of spectra of homonuclear correlation (HOMOCOR) and heteronuclear single-quantum correlation (HSQC).

IR spectra of 6-aryl-1,2,4,5-tetrazinane-3-thiones(ones) contain characteristic absorption bands of NH bonds in the region 3400–3100 cm^{-1}, and also bands of thioamide (C=S) and amide (C=O) bonds at ~1200 and 1680 cm^{-1}.

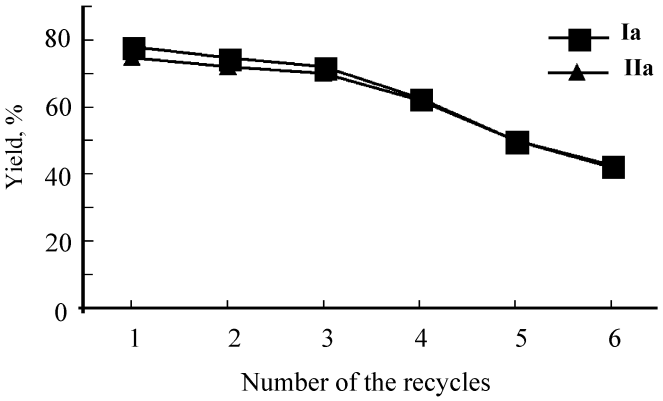


Fig. 2. Yield of 6-aryl-1,2,4,5-tetrazinane-3-thiones(ones) **Ia** and **IIa** at the repeated use of the catalyst $NaHSO_4$–SiO_2.

Table 2. Chemical shifts in the ^{1}H and ^{13}C NMR spectra of 6-aryl-1,2,4,5-tetrazinane-3-thiones(ones) **Ia–Ih, IIa–IIf**[a]

Compd. no.	H^{6}	$H^{1,5}$	$H^{2,4}$	H_{arom}	Other signals	C^{6}	C=S or C=O	C^{1}_{arom}	C^{2-6} (Ar)	Other signals	Isomers ratio
Ia	4.96 (5.42)	3.9 (3.2)	8.67 (8.46)	7.30–7.44	–	64.9 (68.8)	176.0 (177.6)	140.1	126.9–128.5	–	81/19
Ib	4.95 (5.40)	4.04 (3.65)	8.80 (8.64)	7.32–7.47	–	64.0 (67.3)	176.15 (177.1)	132.6, 138.2	128.8–129.3	–	75/25
Ic	4.94 (5.47)	4.10 (3.61)	8.82 (8.67)	7.32–7.47	–	61.9 (65.6)	176.90 (177.6)	135.5, 136.6	125.9–130.5	–	73/27
Id	4.92 (5.39)	4.02 (2.31)	8.71 (8.42)	7.22–7.41	–	64.0 (67.5)	175.9 (173.3)	135.8, 162.7	128.3–129.1	–	74.5/24.5
Ie	4.91	3.85	8.64	7.13–7.26	2.31 (Me)	64.5	175.9	137.1, 137.3	126.9–128.7	21.0 (Me)	100
If	4.88 (5.34)	3.83 (3.10)	8.61 (8.36)	7.11–7.37	3.81 (OMe)	63.9 (66.8)	175.9 (173.3)	130.8, 157.9	114.0, 128.5–129.1	55.05 (OMe)	77/23
Ig	5.08	3.61	8.58	7.15–7.33	2.09 (Me)	62.2	176.9	135.6, 137.6	125.4–130.3	17.71 (Me)	100
Ih	5.35 (4.92)	3.68 (3.98)	8.65 (8.80)	6.92–7.45	–	67.4 (64.2)	177.0 (176.0)	160.0, 157.4	122.9–137.8	–	71/29
IIa	5.39 (4.99)	2.77 (3.68)	6.82 (7.01)	7.31–7.52	–	68.7 (64.5)	156.2 (155.1)	140.4	127.4–128.3	–	84/16
IIb	5.52 (4.94)	2.90 (3.12)	6.39 (6.57)	7.60–7.76	–	64.0 (67.3)	155.3 (156.1)	132.4, 138.2	128.2–129.3	–	79/21
IIc	5.36 (4.95)	2.98 (3.74)	6.85 (6.88)	7.12–7.51	–	67.8 (63.8)	156.1 (154.9)	136.6, 162.8	128.7–129.2	–	69/31
IId	4.92 (5.40)	2.49 (3.52)	6.88 (6.83)	7.11–7.35	2.28 (Me)	64.2 (63.9)	155.0 (154.9)	136.6, 138.6	126.5–128.5	20.5 (Me)	67/33
IIe	4.95 (5.35)	2.70 (3.87)	6.92 (6.86)	7.12–7.33	3.87 (OMe)	63.9 (66.8)	157.9 (158.7)	130.8, 160.3	128.5–130.8	55.0 (OMe)	94/6
IIf	5.53 (5.12)	3.81 (4.18)	7.19 (7.31)	7.53–7.89	–	67.15 (66.85)	155.6 (154.6)	134.1, 147.3	121.8–129.8	–	56/44

[a] Chemical shifts of the minor isomer are given in parentheses.

IR spectra of all compounds lack the band of aldehyde carbonyl group, and the presence of a weak bands of the N–N bonds at 1450 cm^{-1} confirm the formation of 6-aryl-1,2,4,5-tetrazinane-3-thiones(ones). Besides the appearance of the phenyl group vibrations, of those belonging to methine group, and of the overtones combination also supports the formation of the target products.

The ^{1}H NMR spectrum of 6-phenyl-1,2,4,5-tetrazinane-3-thione (**Ia**) (Table 2) shows the presence of two isomers, major and minor. In the spectrum of the major isomer the doublet at 4.96 ppm belongs to the benzyl proton. The triplet signal at 3.90 ppm is due to the presence of NH protons contiguous to the benzyl atom C^{6}. The singlet at 8.67 ppm originates from thioimide protons. The signals of aromatic protons appear in the region 7.30–7.44 ppm

The spectral pattern of the minor isomer is very similar to that of the major. This underlies the assignment of signals of benzyl, amino, and thioimide protons.

Besides to prove the assignment of signals of NH group protons the ^{1}H NMR spectrum was registered after

the addition of D_2O. The protons with the signals at 3.20, 3.90, 8.46, and 8.67 ppm exchanged with D_2O.

In order to confirm the signals assignment we registered the HOMOCOR spectrum of thione **Ia**. The signal at 4.96 ppm gave cross-peaks with the signals at 3.90 and 8.67 ppm. The cross-peak at 3.90 ppm belongs to two protons.

The existence of two thione isomers originates from the difference of their conformations in the solution. In contrast to carbocyclic six-membered systems the tetrazines containing four nitrogen atoms evidently do not exist in the chair conformation due to the interaction between the four unshared electron pairs. In these conformations the phenyl group is located in positions close to axial or equatorial.

The quadrupole moment of the nitrogen atom hampers the calculation of the coupling constants between the protons linked to the nitrogen. It was only possible to measure the coupling constant between the protons NH and H^6, therefore we expected to obtain either a triplet or a doublet of doublets from H^6 protons. However in the ^{1}H NMR spectrum of thione **Ia** we observed only two separate doublets at 4.96 and 5.42 ppm with the spin-spin coupling constants 8.56 and 10.72 Hz respectively. It clearly indicates that protons $H^{1,5}$ are coupled with H^6 protons. If the phenyl group is oriented nearly equatorially then the signal of H^5 proton should be split due to the coupling with H^6, but the proton H^1 cannot couple with it since the dihedral angle is close to 90 deg. In the isomer with the phenyl group in the nearly axial position the signal of H^5 proton is not split by the coupling with H^6, but the proton H^1 couples with the latter. The described analysis of the spectra indicates the presence of two isomers. In the main isomer the phenyl ring is oriented nearly equatorially, and the isomer with the phenyl ring in the position close to axial is the minor one.

In the ^{1}H NMR spectra of the other 6-aryl-1,2,4,5-tetrazinane-3-thiones **Ib–Ih** (Table 2) also two sets of signals were observed of a high and a low intensity (except for the aromatic protons).

The ^{13}C NMR spectrum of 6-phenyl-1,2,4,5-tetrazinane-3-thione (**Ia**) (Table 2) confirms the presence of two isomers, major and minor. In the spectrum of the major isomer the signal at 64.9 ppm belongs to the benzyl carbon atom, at 176.0 ppm, to the carbonyl carbon of the thioamide group. *ipso*-Carbon gives rise to a signal at 140.1 ppm, the other aromatic carbon atoms appear in the region 126.9–128.5 ppm. In the spectra of all compounds synthesized the chemical shifts of the carbon atoms of the phenyl ring are not affected by the conformation of the tetrazinane ring.

The signals of the minor isomer are observed at 68.8 and 177.6 ppm. The spectral pattern of this isomer is nearly identical to that of the major isomer. Therefore these signals were assigned to the benzyl and thioamide carbonyl carbon atoms.

The ^{1}H NMR spectrum of 6-phenyl-1,2,4,5-tetrazinan-3-one (**IIa**) (Table 2) revealed the presence of two isomers, major and minor. In the spectrum of the major isomer the doublet at 5.39 ppm was assigned to the benzyl proton. The triplet at 2.77 ppm belongs to NH protons adjacent to the benzyl carbon atom. The singlet at 6.82 ppm was assigned to imide protons, aromatic protons appeared in the region 7.31–7.58 ppm. The signals of the minor isomer were observed at 4.99, 3.68, and 7.01 ppm. The spectral pattern of this isomer is nearly identical to that of the major isomer. Therefore the observed signals were assigned to the benzyl, imino, and imido protons. A spectrum was also registered under the conditions of exchange with D_2O to prove the positions of NH protons signals. The proton signals at 2.77, 3.68, 6.82, and 7.01 ppm disappeared as a result of the exchange with D_2O.

The ^{13}C NMR spectrum of 6-phenyl-1,2,4,5-tetrazinan-3-one (**IIa**) (Table 2) also indicated the presence of two isomers, major and minor. In the spectrum of the major isomer the signals of the benzyl carbon atom are observed at 68.7 ppm. The signal at 156.2 ppm is due to the presence of the amide carbonyl carbon atom.

ipso-Carbon gives rise to a signal at 140.4 ppm, the other aromatic carbon atoms appear in the region 127.4–128.3 ppm. The signals of the minor isomer were observed at 64.54 and 155.1 ppm. The spectral pattern of this isomer is nearly identical to that of the major isomer. Therefore the observed signals were assigned to the benzyl and amide carbonyl carbon atoms.

To prove the validity of the assignment of signals we registered the HSQC spectrum of compound **IIa**. The signals at 5.39 and 4.99 ppm have cross-peaks at 68.7 and 64.5 ppm.

Therefore as show the ^{1}H and ^{13}C NMR spectra of 6-phenyl-1,2,4,5-tetrazinan-3-ones **IIa—IIf** here the same relationships are observed as in thiones **Ia–Ih**: The compounds as a rule exist as two isomers distinguished by the position of the phenyl ring. In the major isomer it is located close to the equatoirial position, in the minor,

close to the axial position.

Hence we showed for the first time that $NaHSO_4$–SiO_2 in the absence of solvent can efficiently catalyze the one-pot condensation of thiourea (urea), substituted benzaldehyde, and ammonium acetate under the microwave irradiation and at common heating, leading under mild conditions to the formation of new 6-aryl-1,2,4,5-tetrazinane-3-thiones(ones) in an environmentally safe process. We carry on the study in this direction.

EXPERIMENTAL

The reaction progress was monitored and the purity of compounds was checked by TLC on silica gel plates Sigma-Aldrich, layer thickness 250 μm, eluent benzene–EtOAc, 2:8. All melting points were measured in open capillaries and reported uncorrected. IR spectra have been recorded on a spectrophotometer Nicolet-Avatar 360 FT-IR from pellets with KBr; only significant frequency values are reported.

^1H and ^{13}C NMR spectra were registered on a spectrometer Bruker AMX 400 (400 and 100 MHz respectively) in DMSO-d_6. The spectrum of homonuclear correlation (HOMOCOR) and the spectrum of heteronuclear single-quantum correlation (HSQC) were measured on a spectrometer Bruker DRX 500 using the standard parameters. Mass spectra ESI+ve were obtained on a Bruker Daltonic LC-MS instrument. Satisfactory microanalyses were obtained on a CHN-analyzed Carlo Erba 1106. The microwave irradiation was performed using a domestic microwave oven with a rotating disk (LG, MG-395 WA, 760 W).

6-Aryl-1,2,4,5-tetrazinane-3-thiones(ones). *a*. A mixture of 10 mmol of thiourea (urea), 10 mmol of substituted benzaldehyde, 20 mmol of ammonium acetate, and 100 mg $NaHSO_4$–SiO_2 was placed in a bath filled with alumina, the mixture was thoroughly stirred with a glass rod for 19 s, then it was subjected to microwave irradiation at the power 320W for an interval indicated in Table 1 (TLC monitoring). On the completion of the reaction the reaction mixture was extracted with ethyl acetate (3 × 5 ml). The catalyst was filtered off and used repeatedly. The combined extracts were evaporated in a vacuum, the residue was purified by column chromatography, eluent benzene–ethyl acetate, 2:8.

b. The flask with a mixture of reagents was placed in an oil bath and heated at 75°C for the time indicated in Table 1, the workup was performed as described in *a*.

6-Phenyl-1,2,4,5-tetrazinane-3-thione (Ia), mp 187–188°C. IR spectrum, ν, cm^{-1}: 3398, 3211, 3162, 3033, 2896, 1521, 1450, 1178, 700. Found, %: C 49.52; H 5.13; N 28.86. M^+ 195. $C_8H_{10}N_4S$. Calculated, %: C 49.48; H 5.15; N 28.86. *M* 194.25.

6-(4-Chlorophenyl)-1,2,4,5-tetrazinane-3-thione (Ib), mp 170–172°C. IR spectrum, ν, cm^{-1}: 3388, 3228, 3180, 3054, 2967, 1593, 1489, 1166, 821. Found, %: C 42.03; H 3.95; N 24.51. M^+ 229. $C_8H_9ClN_4S$. Calculated, %: C 42.01; H 3.97; N 24.50. *M* 228.70.

6-(2-Chlorophenyl)-1,2,4,5-tetrazinane-3-thione (Ic), mp 158–160°C. IR spectrum, ν, cm^{-1}: 3368, 3240, 3186, 3058, 2968, 1588, 1480, 818. Found: M^+ 229. $C_8H_9ClN_4S$. Calculated: *M* 228.70.

6-(4-Fluorophenyl)-1,2,4,5-tetrazinane-3-thione (Id), mp 170–172°C. IR spectrum, ν, cm^{-1}: 3380, 3245, 3199, 3067, 2920, 1541, 1450, 1178, 779. Found, %: C 45.29; H 4.25; N 26.41. M^+ 212. $C_8H_9FN_4S$. Calculated, %: C 45.27; H 4.27; N 26.40. *M* 212.24.

6-(4-Tolyl)-1,2,4,5-tetrazinane-3-thione (Ie), mp 146–148°C. IR spectrum, ν, cm^{-1}: 3368, 3198, 3166, 3065, 2920, 1538, 1460, 1175, 768. Found, %: C 51.92; H 5.79; N 26.92. M^+ 209. $C_9H_{12}N_4S$. Calculated, %: C 51.90; H 5.81; N 26.90. *M* 208.28.

6-(4-Methoxyphenyl)-1,2,4,5-tetrazinane-3-thione (If), mp 170–174°C. IR spectrum, ν, cm^{-1}: 3316, 3211, 3168, 3071, 2933, 1510, 1463, 1174, 835. Found, %: C 48.19; H 5.37; N 24.96. M^+ 225. $C_9H_{12}N_4OS$. Calculated, %: C 48.20; H 5.39; N 24.96. *M* 224.28.

6-(2-Tolyl)-1,2,4,5-tetrazinane-3-thione (Ig), mp 160–164°C. IR spectrum, ν, cm^{-1}: 3320, 3216, 3153, 3065, 2920, 1538, 1463, 1175, 760. Found: M^+ 209. $C_9H_{12}N_4S$. Calculated: *M* 208.28.

6-(3-Phenoxyphenyl)-1,2,4,5-tetrazinane-3-thione (Ih), mp 148–150°C. IR spectrum, ν, cm^{-1}: 3407, 3171, 3039, 2902, 1543, 1450, 1248, 783. Found, %: C 58.70; H 4.92; N 19.55. M^+ 287. $C_{14}H_{14}N_4OS$. Calculated, %: C 58.72; H 4.93; N 19.57. *M* 286.35.

6-Phenyl-1,2,4,5-tetrazinan-3-one (IIa), mp 192–194°C. IR spectrum, ν, cm^{-1}: 3398, 3211, 3162, 3033, 2896, 1521, 1450, 1178, 700. Found, %: C 53.95; H 5.60; N 31.50. M^+ 179. $C_8H_{10}N_4O$. Calculated, %: C 53.93; H 5.61; N 31.46. *M* 178.19.

6-(4-Chlorophenyl)-1,2,4,5-tetrazinan-3-one (IIb), mp 180–181°C. IR spectrum, ν, cm^{-1}: 3388, 3228, 3180, 3054, 2967, 1593, 1489, 1166, 821. Found, %: C 45.16; H 4.24; N 16.65. M^+ 213. $C_8H_9ClN_4O$. Calculated, %: C 45.16; H 4.27; N 16.67. *M* 212.64.

6-(4-Fluorophenyl)-1,2,4,5-tetrazinan-3-one (IIc), mp 150–152°C. IR spectrum, ν, cm^{-1}: 3368, 3240, 3186, 3058, 2968, 1588, 1480, 818. Found: M^+ 197. $C_8H_9FN_4O$. Calculated: *M* 196.18.

6-(4-Tolyl)-1,2,4,5-tetrazinan-3-one (IId), mp 176–178°C. IR spectrum, ν, cm^{-1}: 3380, 3245, 3199, 3067, 2920, 1541, 1450, 1178, 779. Found, %: C 56.28; H 6.22; N 29.19. M^+ 193. $C_9H_{12}N_4O$. Calculated, %: C 56.25; H 6.25; N 29.16. *M* 192.22.

6-(4-Methoxy)-1,2,4,5-tetrazinan-3-one (IIe), mp 160–162°C. IR spectrum, ν, cm^{-1}: 3368, 3198, 3166, 3065, 2920, 1538, 1460, 1175, 768. Found, %: C 51.95; H 5.26; N 26.95. M^+ 209. $C_9H_{12}N_4S$. Calculated, %: C 51.92; H 5.28; N 26.92. *M* 208.22.

6-(3-Nitrophenyl)-1,2,4,5-tetrazinan-3-one (IIf), mp 188–190°C. IR spectrum, ν, cm^{-1}: 3316, 3211, 3168, 3071, 2933, 1510, 1463, 1174, 835. Found, %: C 43.01; H 4.04; N 31.35. M^+ 224. $C_8H_9N_5O_3$. Calculated, %: C 43.05; H 4.06; N 31.38. *M* 223.19.

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