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Reaction of 4-Aryl-3-thiosemicarbazides with Phenylisothiocyanate: A Facile Synthesis of Thiazole, Pyrazole and Pyrimidine Derivatives

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The reaction of 4-aryl-3-thiosemicarbazides **1a-d** with phenylisothiocyanate gave the intermediate potasium salts **2a-d**. The latter afforded **3a-d**, **13a-d** and **19** upon the reaction with phenacyl bromide, monochloroacetic acid and ethyl bromocyanoacetate respectively.

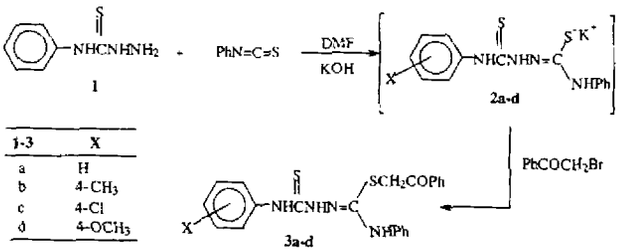
INTRODUCTION

The reactivity of 4-aryl-3-thiosemicarbazides towards ketones, dimeric adducts and α-haloketones followed by in situ heterocyclization of the resulting adducts with various reagents has been recently studied by our research group[1-4] to give a variety of polyfunctionally substituted thiazole, pyridine and pyrazole derivatives. The latter compounds are of interest because of their wide spectrum of biological properties and applications; they have been used as dihydrofolate reductase inhibitors as well as antitumor agents.[5] Some of them have shown antimicrobial activity,[6] diuretic properties,[7] activity against platelet aggregation,[8] and antidiabetic activity.[9,10] In addition they have proved to be convenient candidates for chemical transformations into various fused heterocyclic ring systems. Prompted by our earlier promising results, we extended our work to investigate the use of 4-aryl-3-thiosemicarbazides for the formation of thiazole derivatives through their reactions with phenylisothiocyanate in basic dimethylformamide followed by the reaction with α-haloketones.

RESULTS AND DISCUSSION

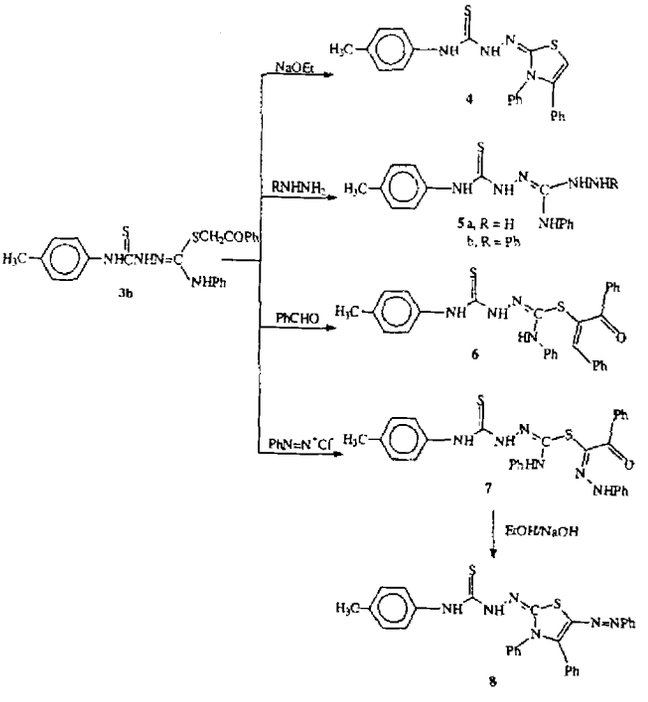
The reaction of 4-aryl-3-thiosemicarbazide derivatives **1a-d**[11] with phenylisothiocyanate in dimethylformamide containing potassium hydroxide afforded the intermediate potassium sulphide salts **2a-d**. The reaction of those intermediates with phenacyl bromide gave the thioether derivatives **3a-d**.

The structures of **3a-d** were established on the basis of analytical and spectral data. Further confirmations for structures of **3a-d** were obtained through studying the chemical reactivity of **3b** towards chemical reagents. Thus, compound **3b** underwent cyclization readily when heated in



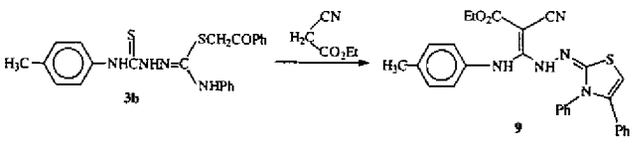
1-3	X
a	H
b	4-CH_3
c	4-Cl
d	4-OCH_3

sodium ethoxide solution to afford the thiazole derivative **4**, and its formation is explained in terms of wafer elimination. Also the reaction of **3b** with both of hydrazine hydrate and phenylhydrazine gave the hydrazino derivatives **5a,b**. The latter products were formed *via* loss of the thioether moiety by the effect of hydrazine. Moreover, the reaction of **3b**



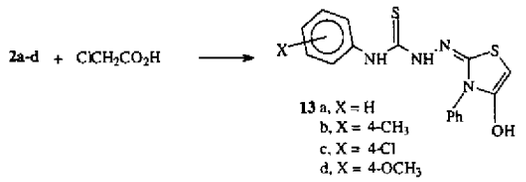
with benzaldehyde afforded the benzal derivative **6**. When compound **3b** was coupled with benzenediazonium chloride in ethanol containing sodium acetate solution, it gave the phenylhydrazone derivative **7** that was cyclized readily by heating in ethanol containing sodium hydroxide solution to give the thiazole derivative **8**. Structures of compounds **4-8** were confirmed based on the analytical and spectral data.

The reactivity of **3b** towards cyanomethylene reagents was studied. The reaction of **3b** with ethyl cyanoacetate gave the thiazole derivative **9**. Structure of **9** was based on analytical and spectral data. However ^{1}H NMR spectrum showed the presence of a triplet at δ_H 1.16 for ester methyl group, a singlet at δ_H 2.21 for CH_3 group, a quartet at δ_H 4.24 for ester CH_2 group, a singlet at δ_H 6.92 ppm for thiazole H-5; a multiplet at δ_H 7.32-7.53 for C_6H_5 and C_6H_4 protons and two D_2O exchangeable singlets at δ_H 8.32, 8.73 for two NH groups.

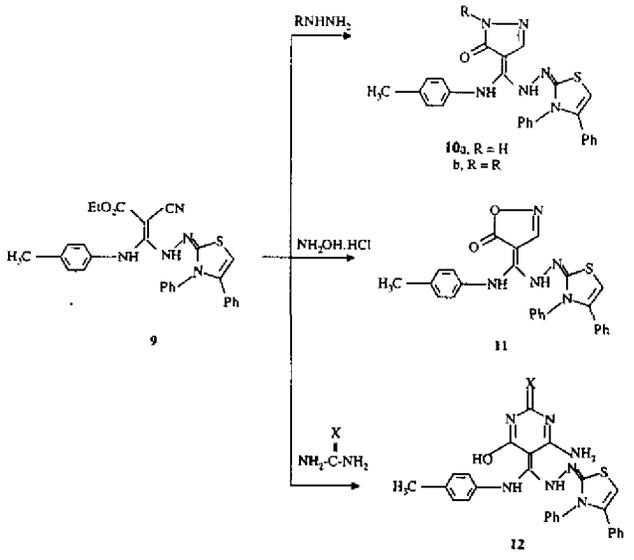


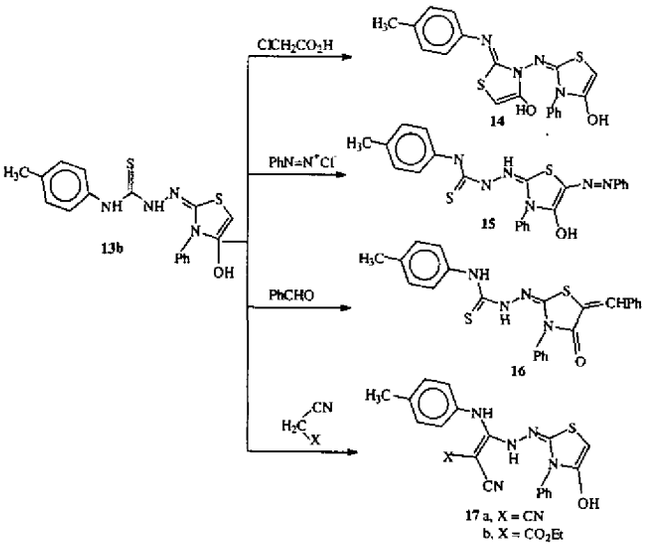
The reaction of **9** with each of hydrazine hydrate and phenylhydrazine yielded the pyrazole derivatives **10a,b**. The reaction of **9** with hydroxylamine hydrochloride gave the isoxazole-5-one derivative **11**. On the other hand, the reaction of compound **9** with both of urea and thiourea in sodium ethoxide solution gave the pyrimidine derivatives **12a,b**. Structures of the latter products were established on the basis of analytical and spectral data (see experimental section). For example the ^{1}H NMR spectrum of **12a** showed the presence of a singlet at δ_H 2.23 for CH_3 group; a singlet at δ_H 4.21 for NH_2 group; a singlet at δ_H 6.66 for thiazole H-5; a multiplet at δ_H 7.33-7.46 for two C_6H_5, two singlets (D_2O exchangeable) at δ_H 8.34, 8.45 for two NH groups and a singlet at δ_H 10.30 for OH group.

Next, when we studied the reaction of the intermediate sulphide salts **2a-d** with monochloroacetic acid, the reaction led to the formation of the thiazole-4-hydroxy derivatives **13a-d**. Structures of the products were assigned on the basis of their analytical and spectral data.



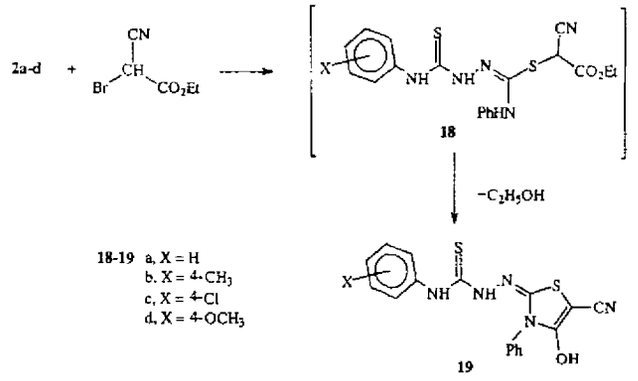
The reaction of **2a-d** with ethyl bromocyanoacetate[12] gave the thiazole derivatives **13a-d**, the structure of which were established on the basis of analytical and spectral data. Further confirmation for the structure of **13b** (as an example) was obtained through studying its chemical reactivity towards some chemical reagents. Thus, the reaction of **13b** with another molecule of monochloroacetic acid in ethanol solution under reflux produced the dithiazol-4-hydroxy derivative **14**. Also when compound **13b** was coupled with bezenediazonium chloride in ethanol containing sodium acetate, it yielded the phenylazo derivative **15**. Moreover, the reaction of **13b** with benzaldehyde gave the benzal derivative **16**. Furthermore, the reaction of **13b** towards two cyano methylene derivatives produced the corresponding condensed products **17a,b**. The analytical and spectral date obtained for compounds **14-17** are coincident with the as-



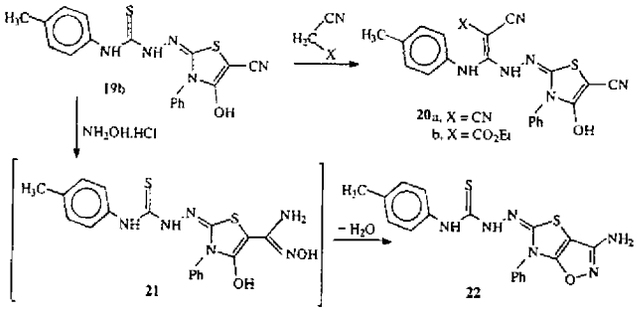


signed structures.

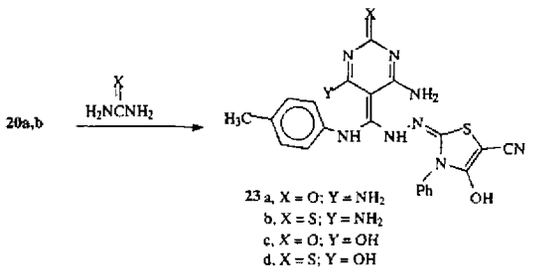
The reaction of the intermediate potassium sulphide salts **2a-d** with bromoethyl cyano acetate gave the thiazole derivatives **19a-d**. The reaction took place *via* the intermediate formation of **18a-d** which was then followed by ethanol elimination. The structures of **19a-d** were assigned on the basis of their analytical and spectral data. The IR spectrum of **19b** showed the presence of OH group stretching at ν_{max} = 3560-3365 cm^{-1} and CN group stretching at ν_{max} = 2220 cm^{-1}. Moreover, the ^1H NMR spectrum showed the presence of a singlet at δ_H 2.22 for CH_3 group; a multiplet at δ_H 7.32-7.41 for C_6H_5 and C_6H_4 groups, two singlets at δ_H 8.21, 8.42 for 2NH groups and a singlet at δ_H 10.30 for OH group.



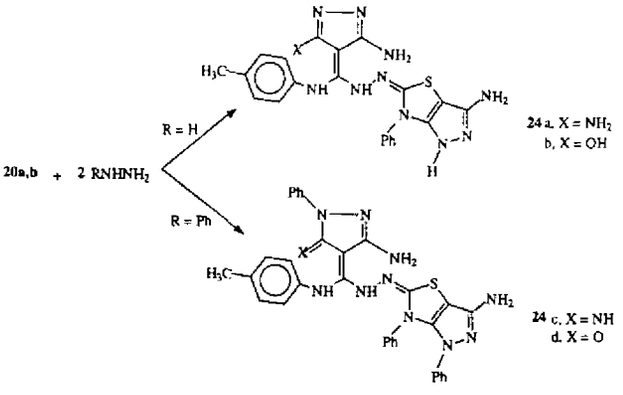
The reaction of **19b** with each of malononitrile and ethyl cyanoacetate gave the condensed products **20a,b**, respectively. Moreover, the reaction of **19b** with hydroxylamine hydrochloride afforded the isoxazolo[5,4-d]thiazole derivative **22**. Formation of **22** was explained in terms of the formation of the amidoxime intermediate **21** followed by eliminating molecular water.



The reactivity of both **20a,b** towards chemical reagents was studied. Thus, compounds **20a,b** reacted with both urea and thiourea to give the corresponding pyrimidine derivatives **23a-d**.



The reaction of **20a,b** with two fold of both hydrazine hydrate and phenylhydrazine to yield the corresponding pyrazolo[3,4-d]thiazole derivatives **24a-d**.



CONCLUSION

The reaction of 4-aryl-3-thiosemicarbazides with phenyl isothiocyanate gives intermediates which are readily heterocyclized when treated with a variety of α-halocarbonyl compounds to give a series of heterocyclic and fused heterocyclic derivatives. The compounds thus prepared may be of interest to investigators working in related areas of heterocyclic chemistry and may be studied furher for biological activity.

EXPERIMENTAL

All melting points were uncorrected. IR spectra were recorded (KBr) on a pye Unicame SP - 1000 spectrophotometer. ^1H NMR spectra were recorded on a Varian EM - 390-90 MHz and in CD_3SOCD_3 as a solvent using TMS as internal reference. Chemical shifts are expressed as δ_H units (ppm). Analytical data were obtained from the Micro Analytical Data Center at Cairo University.

1-[Benzoylmethylsulphido-phenylaminocarbonyl]-4-phenyl-3-thiosemicarbazone 3a

1-[Benzoylmethylsulphido-phenylaminocarbonyl]-4-(p-tolyl)-3-thiosemicarbazone 3b
1-[Benzoylmethylsulphido-phenylaminocarbonyl]-4-(p-chloro)-3-thiosemicarbazone 3c
1-[Benzoylmethylsulphido-phenylaminocarbonyl]-4-(p-methuxy)-3-thiosemicarbazone 3d
4-Hydroxy-3-phenyl-2-[4-phenyl-3-thiosemicarbazono]-thiazole-2-ylidene 13a
4-Hydroxy-3-phenyl-2-[4-(p-tolyl)-3-thiosemicarbazono]-thiazole-2-ylidene 13b
4-Hydroxy-3-phenyl-2-[4-(p-chloro)-3-thiosemicarbazono]thiazole-2-ylidene 13c
4-Hydroxy-3-phenyl-2-[4-(p-methoxy)-3-thiosemicarbazono]thiazole-2-ylidene 13d
5-Cyano-4-hydroxy-3-phenyl[4-phenyl-3-thiosemicarbazono]thiazole-2-ylidene 19a
5-Cyano-4-hydroxy-3-phenyl[4-(p-tolyl)-3-thiosemicarbazono]thiazole-2-ylidene 19b
5-Cyano-4-hydroxy-3-phenyl[4-(p-chloro)-3-thiosemicarbazono]thiazole-2-ylidene 19c
5-Cyano-4-hydroxy-3-phenyl[4-p-methoxy)-3-thiosemicarbazono]thiazole-2-ylidene 19d

General Procedure

To a solution of each of **1a-d** (0.01 mol) in dimethylformamide (30 mL), phenylisothiocyanate (1.35 mL, 0.01 mol) and potassium hydroxide (0.56 g, 0.01 mol) were added. The mixture was kept at room temperature overnight and then was added, to either phenacyl bromide (1.99 g, 0.01 mol), in case of synthesis of **3a-d**, or monochloroacetic acid (0.94 g, 0.01 mol), in case of synthesis of **13a-d**, or ethyl bromocyanoacetate [prepared by adding bromine (0.79 g, 0.01 mol) to ethylcyanoacetate (91.13 mL, 0.01 mol)], in case of synthesis of **19a-d**. Also the reaction mixture was kept at room temperature overnight. The solid product formed in each case upon dilution with dilute aqueous HCl solution was collected by filtration.

3,4-Diphenyl-2-[4-(p-tolyl)-3-thiosemicarbazono]thiazole-2-ylidene 4

A suspension of **3b** (4.34 g, 0.01 mol) in sodium ethoxide [prepared by adding sodium metal (0.23 g, 0.01 mol) to absolute ethanol, 50 mL] was heated in a boiling water bath for 4 hrs. Then the reaction mixture was left et room temperature and poured into ice/water containing a few drops of hydrochloric acid (pH = 6). The solid product so formed was collected by filtration.

1-Hydrazinocarbonyl-1-phenylamino-4-(p-tolyl)-3-thiosemicarbazone 5a
1-Phenylamino-1-phenylhydrazinocarbonyl-4-(p-tolyl)-3-thiosemicarbazone 5b

General Procedure

Either hydrazine hydrate or phenylhydrazine (0.01 mol) was added to a solution of **3b** (4.34 g, 0.01 mol) in DMF (30 mL). The reaction mixture was heated under reflux for 3 h. The solid product formed upon dilution with water containing a few drops of hydrochloric acid, was collected by filtration.

1-[1-Benzoyl-2-phenyl-1-sulphidovinyl]phenylaminocarbonyl-4-(p-tolyl)-3-thiosemicarbazone 6
5-Benzalo-4-oxo-3-phenyl-4-(p-tolyl)-3-thiosemicarbazonothiazol-2-ylidene 16

General Procedure

To a solution of either **3b** (4.34 g, 0.01 mol) in DMF (40 mL) or **13b** (3.56 g, 0.01 mol) in dioxane (30 mL), a few drops of piperidine and benzaldehyde (1.06 g, 0.01 mol) were added. The reaction mixture was heated under reflux for 6 h and then evaporated *in vacuo*. The residue was triturated with diethyl ether and the solid product formed was collected by filtration.

3-[4-Hydroxythiazolo]-4-(p-tolyl)semicarbazono]-4-hydroxy-3-phenylthiazole-2-ylidene 14

To a solution of **13b** (3.56 g, 0.01 mol) in ethanol (30 mL), monochloroacetic acid (0.94 g, 0.01 mol) was added. The reaction mixture was heated under reflux for 3 h. The solid product formed upon dilution with water containing a few drops of hydrochloric acid was collected by filtration.

1-[2-Hydrazonoacetophenyl-1-benzoyl-1-sulphidovinyl]-phenylaminocarbonyl-4-(p-tolyl)-3-thiosemicarbazone 7
4-Hydroxy-3-phenyl-5-phenylazo-4-(p-tolyl)-3-thiosemicarbazonethiazole-2-ylidene 15

General Procedure

To a cold solution (0-5 °C) either **3b** (4.34 g, 0.01 mol) or **13b** (3.5 g, 0.01 mol) in ethanol, 50 mL, containing sodium acetate, 6 g, benzenediazonium chloride (0.01 mol) [prepared by adding sodium nitrite solution (0.04 g, 0.01 mol) to a cold solution of aniline (0.93 g, 0.01 mol) containing the appropriate quantity of hydrochloric acid] was added with continuous stirring. The reaction mixture was stirred at room temperature for 4 h. The solid product formed was collected by filtration.

3,4-Diphenyl-5-phenylhydrazono-2-[4-(p-tolyl)]-3-thiosemicarbazono]thiazole-2-ylidene 8

To a solution of **7** (5.38 g, 0.01 mol) in ethanol, 50 mL, sodium hydroxide (0.39 g, 0.01 mol) was added. The reaction mixture was heated under reflux for 1 h. The solid product formed upon dilution with water containing a few drops of hydrochloric acid was collected by filtration.

2-[3-Ethoxycarbonylcyanomethinoylideno-4-(p-tolyl)]-semicarbazono-3,4-diphenylthiazolo-2-ylidene 9
[3-Malononitrilo-4-(p-tolyl)-2-ylideno]semicarbazono-[4-hydroxy-3-phenyl]thiazole-2-ylidene 17a
[3-Ethylcyanoacetato-4-(p-tolyl)-2-ylideno]semicarbazono-[4-hydroxy-3-phenyl]thiazole-2-ylidene 17b
[3-Malononitrilo-4-(p-tolyl)-2-ylideno]semicarbazono-[5-cyano-4-hydroxy-3-phenyl]thiazole-2-ylidene 20a
[3-Ethylcyanoacetato-4-(p-tolyl)-2-ylideno]semicarbazono-[5-cyano-4-hydroxy-3-phenyl]thiazole-2-ylidene 20b

General Procedure

To a solution of either of **3b**, **13b** or **19b** (0.01 mol) in DMF (30 mL) containing a few drops of piperidine, ethyl cyanoacetate (1.13 g, 0.01 mol) or malononitrile (0.66 g, 0.01 mol) was added. The reaction mixture was heated under reflux for 6 h. The solid product formed was collected by filtration.

2-[3-(3-Amino-5-oxo-[1H]pyrazolo-4-ylideno]-4-(p-tolyl)-semicarbazono-3,4-diphenylthiazole-2-ylidene 10a
2-[3-(3-Amino)-5-oxo-1-phenylpyrazolo-4-ylideno]-4-(p-tolyl)semicarbazono-3,4-diphenylthiazole-2-ylidene 10b
3-[3,5-Diamino-[2H]-pyrazolo-4-ylideno]-4-(p-tolyl)semicarbazono-6-amino-3-phenyl-[4H]-pyrazolo[3,4-d]thiazole-2-ylidene 24a
3-[3,5-Diamino-2-phenylpyrazolo-4-ylideno]-4-(p-tolyl)-semicarbazono-6-amino-3,4-diphenylpyrazolo[3,4-d]thiazole-2-ylidene 24b
3-[5-Amino-3-oxo-[2H]-pyrazolo-4-ylideno]-4-(p-tolyl)-semicarbazono[3-phenyl-6-amino-[4H]-pyrazolo[3,4-d]-thiazole-2-ylidene 24c
3-[5-Amino-3-oxo-2-phenylpyrazolo-4-ylideno]-4-(p-tolyl)semicarbazono[3,4-diphenyl-6-aminopyrazolo[3,4-d]thiazole-2-ylidene 24d

General Procedure

To a solution of either of **9** or **23a,b** (0.01 mol) in DMF (30 mL), hydrazine hydrate or phenylhydrazine (0.01 mol) was added. The reaction mixture was heated under reflux for 3 h. The solid product formed upon dilution with water containing a few drops of hydrochloric acid was collected by filtration.

3-[5-Amino-3-oxoisoxazolo-4-ylideno]-4-(p-tolyl)semicarbazono-3,4-diphenylthiazole-2-ylidene 11
6-Amino-3-phenyl-2-[4-(p-tolyl)-3-thiosemicarbazono]-isoxazolo[5,4-d]thiazole 22

General Procedure

To a solution of **9** or **19b** (0.01 mol) in dioxane (30 mL) containing sodium acetate (4 g), (0.69 g, 0.01 mol) hydroxylamine hydrochloride was added. The reaction mixture was heated under reflux for 3 h. The solid product formed upon dilution with ice/water was kept at room temperature for 4 h and then collected by filtration.

3-[6-Amino-4-hydroxy-2-oxo-pyrimidino-5-ylideno]-4-(p-tolyl)semicarbazono-3,4-diphenylthiazole-2-ylidene 12a
3-[6-Amino-4-hydroxy-2-thieno-pyrimidino-5-ylideno]-4-(p-tolyl)semicarbazono-3,4-diphenylthiazole-2-ylidene 12b
3-[4,6-Diamino-2-oxo-pyrimidino-5-ylideno]-4-(p-tolyl)-semicarbazono[5-cyano-4-hydroxy-3-phenyl]thiazolo-2-ylidene 23a
3-[4,6-Diamino-2-thiopyrimidino-5-ylideno]-4-(p-tolyl)-semicarbazono[5-cyano-4-hydroxy-3-phenyl]thiazolo-2-ylidene 23b
3-[6-Amino-4-hydroxy-2-oxo-pyrimidino-5-ylideno]-4-(p-tolyl)semicarbazono[5-cyano-4-hydroxy-3-phenyl]thiazole-2-ylidene 23c
3-[6-Amino-4-hydroxy-2-thienopyrimidino-5-ylideno]-4-(p-tolyl)semicarbazono[5-cyano-4-hydroxy-3-phenyl]thiazole-2-ylidene 23d

General Procedure

To a solution of **9** or **20a,b** (0.01 mol) in DMF (5 mL), sodium ethoxide solution [prepared by adding sodium metal (0.23 g, 0.01 mol) to absolute ethanol (50 mL)] was added. The reaction mixtures were treated with either urea or thiourea (0.01 mol), then heated in a boiling water bath for 5 h. The solid product formed upon pouring into ice/water containing a few drops of hydrochloric acid was collected by filtration.

Table 1. Physical and Analytical Data of the Newly Prepared Compounds

Compd No.	Solvent	M.P. (°C)	Yield (%)	Mol. Formula (Mol. wt.)	Analysis (Calcd./Found) % C	H	N	S
3a	Dioxan	180	80	$C_{22}H_{20}N_4OS_2$	62.84	4.79	13.32	
				(420.23)	62.80	4.75	13.30	15.20
3b	Dioxan	180	80	$C_{23}H_{22}N_4OS_2$	63.57	5.10	12.89	14.76
				(434.51)	63.55	5.10	12.87	14.74
3c	Dioxan	185	80	$C_{22}H_{19}N_4OS_2Cl$	58.08	4.21	12.31	14.09
				(454.89)	58.06	4.20	12.30	14.05
3d	Dioxan	190	80	$C_{23}H_{22}N_4O_2S_2$	60.31	4.92	12.73	14.63
				(438.61)	60.31	4.70	12.42	14.53
4	Dioxan	215	80	$C_{23}H_{20}N_4S_2$	66.32	4.84	13.45	15.40
				(416.37)	66.30	4.82	13.43	15.30
5a	Dioxan	90	75	$C_{15}H_{18}N_6S$	57.31	5.77	26.73	10.20
				(314.58)	57.30	5.77	26.71	10.20
5b	Dioxan	120	73	$C_{21}H_{22}N_6S$	64.60	5.67	21.52	8.21
				(390.45)	64.60	5.65	21.50	8.20

6	Dioxan	130	74	$C_{30}H_{26}N_4OS_2$	68.94	5.01	10.72	12.27
				(522.31)	68.92	5.00	10.70	12.26
7	EtOH	90	79	$C_{29}H_{26}N_6OS_2$	64.66	4.86	15.60	11.91
				(538.40)	64.64	4.84	15.60	11.90
8	EtOH	180	83	$C_{29}H_{24}N_6S_2$	66.90	4.64	16.14	12.32
				(520.50)	66.90	4.62	16.12	12.31
9	Dioxan	185	82	$C_{28}H_{25}N_5O_2S$	67.86	5.08	14.13	6.47
				(495.38)	67.86	5.08	14.12	6.45
10a	Dioxan	110	78	$C_{26}H_{23}N_7OS$	64.85	4.81	20.36	6.66
				(481.47)	64.75	4.71	20.26	6.46
10b	Dioxan	197	77	$C_{32}H_{27}N_7OS$	68.92	4.88	17.58	5.75
				(557.28)	68.92	4.86	17.56	5.72
11	Dioxan	97	76	$C_{26}H_{22}N_6O_2S$	64.72	4.59	17.42	6.64
				(482.51)	64.71	4.58	17.40	6.63
12a	EtOH	180	82	$C_{27}H_{23}N_7O_2S$	63.64	4.55	19.24	6.29
					63.62	4.52	19.21	6.27
12b	EtOH	152	81	$C_{27}H_{25}N_7OS_2$	61.70	4.41	18.65	12.20
					61.69	4.40	18.55	12.18
13a	Dioxan	230	85	$C_{16}H_{14}N_4OS_2$	56.12	4.12	16.36	18.73
					56.02	4.11	16.29	18.63
13b	Dioxan	180	87	$C_{17}H_{16}N_4OS_2$	57.28	4.52	15.72	17.99
					57.20	4.50	15.70	17.95
13c	Dioxan	180	85	$C_{16}H_{13}N_4OS_2Cl$	51.00	3.47	14.87	17.02
					51.00	3.45	14.85	17.00
13d	Dioxan	140	86	$C_{17}H_{16}N_4O_2S_2$	54.82	4.33	15.04	17.22
					54.72	4.32	15.04	17.02
14	Dioxan	130	83	$C_{19}H_{16}N_4O_2S_2$	57.56	4.06	14.13	16.18
					57.46	4.00	14.12	16.09
15	Dioxan	80	80	$C_{23}H_{20}N_6OS_2$	59.98	4.37	18.25	13.92
					59.72	4.36	18.14	13.79
16	EtOH	210	74	$C_{24}H_{20}N_4OS_2$	64.84	4.53	12.60	14.43
					64.84	4.52	12.60	14.41
17a	EtOH	210	78	$C_{20}H_{16}N_6OS$	61.84	4.15	21.64	8.26
					61.74	4.05	21.46	8.24
17b	DMF	180	77	$C_{22}H_{21}N_5O_2S$	60.68	4.86	16.08	7.36
					60.62	4.75	16.00	7.34
19a	Dioxan	160	85	$C_{17}H_{13}N_5OS_2$	55.57	3.56	19.06	17.45
					55.50	3.54	19.04	17.42
19b	EtOH	200	90	$C_{18}H_{15}N_5OS_2$	56.68	3.96	18.36	16.81
					56.65	3.86	18.36	16.80
19c	EtOH	200	85	$C_{17}H_{12}N_5OS_2Cl$	50.81	3.01	17.43	15.96
					50.49	3.00	17.24	15.79
19d	EtOH	180	83	$C_{18}H_{15}N_5O_2S_2$	54.40	3.80	17.62	16.13
					54.00	3.79	17.61	16.12
20a	EtOH	180	79	$C_{21}H_{15}N_7OS$	61.01	3.65	23.71	7.76
					61.00	3.62	23.49	7.54
20b	EtOH	180	82	$C_{22}H_{20}N_6O_2S$	60.00	4.37	18.25	6.96
					60.00	4.36	18.23	6.88
22	Dioxan	200	78	$C_{18}H_{16}N_6OS_2$	54.53	4.06	21.20	16.17
					54.52	4.02	21.12	16.01
23a	$CHCl_3$	110	81	$C_{22}H_{19}N_9O_2S$	55.81	4.04	26.62	6.77
					55.60	4.02	26.41	6.52
23b	Dioxan	160	80	$C_{27}H_{19}N_9OS_2$	53.98	3.91	25.75	13.10
					53.80	3.89	25.69	13.00
23c	DMF	110	83	$C_{22}H_{18}N_8O_3S$	55.69	3.82	23.62	6.76
					55.62	3.80	23.62	6.75
23d	DMF	140	79	$C_{22}H_{18}N_8O_2S_2$	53.87	3.70	22.84	13.07
					53.87	3.70	22.80	13.00
24a	EtOH	252	78	$C_{21}H_{22}N_{11}S$	54.77	4.81	33.46	6.96
					54.61	4.71	33.20	6.95
24b	DMF	270	77	$C_{33}H_{30}N_{11}S$	64.69	4.93	25.15	5.23
					64.64	4.92	25.10	5.20
24b	DMF	270	77	$C_{33}H_{30}N_{11}S$	64.69	4.93	25.15	5.23
					64.64	4.92	25.10	5.20
24c	DMF	254	79	$C_{21}H_{20}N_{10}OS$	54.77	4.37	30.42	6.96
					54.75	4.36	30.42	6.95
24d	DMF	230	83	$C_{33}H_{28}N_{10}OS$	64.69	4.60	22.86	5.23
					64.68	4.60	22.74	5.21

Table 2. IR and ^{1}H NMR Data of the Newly Prepared Compounds

Compd No.	IR cm^{-1} (selected bands)	^{1}H NMR (δ ppm)
3a	3460-3330 (3NH), 3100 (CH. aromatic), 2890 (CH_2), 1690 (C=O), 1210-1190 (C=S).	5.21 (s, 2H, CH_2), 7.31-7.48 (m, 15H, 3 aromatic-H), 8.22, 8.34, 8.40 (3s, 3H, 3NH).
3b	3460-3350 (3NH), 3060 (CH. aromatic), 2890, 2890 (CH_3, CH_2), 1685 (C=O), 1220-1210 (C=S).	2.21 (s, 3H, CH_3), 5.32 (s, 2H, CH_2), 7.21-7.46 (m, 14H, aromatic-H), 8.21, 8.60, 8.73 (3s, 3H, 3NH).
3c	3460-3330 (3NH), 3100 (CH. aromatic), 2890 (CH_2), 1690 (C=O), 1210-1190 (C=S).	5.09 (s, 2H, CH_2), 7.32-7.51 (m, 14H, aromatic-H), 8.32, 8.43, 8.80 (3s, 3H, 3NH).
3d	3470-3335 (3NH), 3060 (CH. aromatic), 2980, 2890 (CH_3, CH_2), 1690 (C=O), 1210-1190 (C=S).	3.79 (s, 3H, CH_3), 5.28 (s, 2H, CH_2), 7.33-7.47 (m, 14H, aromatic-H), 8.35, 8.40, 8.48 (3s, 3H, 3NH).
4	3455-3380 (2NH), 3065 (CH. aromatic), 2985(CH_3), 1660 (C=N), 1220-1190 (C=S).	2.24 (s, 3H, CH_3), 6.67 (s, 1H, thiazole H-5), 7.30-7.51 (m, 14H, aromatic-H), 8.35, 8.40 (2s, 2H, 2NH).
5a	3470-3370 (4NH, NH_2), 3065 (CH. aromatic), 2985 (CH_3), 1655 (C=N), 1200 (C=S).	2.24 (s, 3H, CH_3), 5.39 (br s, 2H, NH_2), 7.32-7.51 (m, 9H, aromatic-H), 8.29-8.34, 9.21 (4br s, 4H, 4NH).
5b	3450-3380 (5NH), 3060 (CH. aromatic), 2985 (CH_3), 1660 (C=N), 1200-1195 (C=S).	2.23 (s, 3H, CH_3), 7.32-7.48 (m, 14H, aromatic-H), 8.31-8.35, 8.49 (m, 5H, 5NH).
6	3470-3380 (3NH), 3050 (CH. aromatic), 2975 (CH_3), 1695 (C=O), 1665 (C=N), 1640 (C=C), 1215-1200 (C=S).	2.24 (s, 3H, CH_3), 6.89 (s, 1H, CH=C), 7.32-7.48 (m, 19H, aromatic-H), 8.42-8.46 (m, 3H, 3NH).
7	3480-3360 (4NH), 3060 (CH. aromatic), 2970 (CH_3), 1695 (C=O), 1665 (C=N), 1205 (C=S).	2.28 (s, 3H, CH_3), 7.28-7.46 (m, 19H, aromatic-H), 8.321-8.45, 9.21 (4s, 4H, 4NH).
8	3465-3350 (2NH), 3060 (CH. aromatic), 2970 (CH_3), 1670 (exocyclic C=N), 1205 (C=S).	2.28 (s, 3H, CH_3), 7.31-7.45 (m, 19H, aromatic-H), 8.32, 8.40 (2s, 2H, 2NH).
9	3480-3365 (2NH), 3060 (CH. aromatic), 2975, 2890 (CH_3, CH_2), 2220 (CN), 1680 (C=O), 1665 (exocyclic C=N), 1635 (C=C).	1.16 (t, 3H, ester CH_3), 2.21 (s, 3H, CH_3), 4.24 (q, 2H, OCH_2), 6.92 (s, 1H, thiazole-H), 7.32-7.53 (m, 14H, aromatic-H), 8.32, 8.73 (2s, 2H, 2NH).
10a	3470-3360 (NH_2, 3NH), 3060 (CH. aromatic), 2890 (CH_3), 1685 (C=O), 1665 (exocyclic C=N), 1640 (C=C).	2.20 (s, 3H, CH_3), 5.32 (s, 2H, NH_2), 6.31 (s, 1H, thiazole H-5), 7.32-7.45 (m, 14H, aromatic-H), 8.35, 8.41, 8.73 (3s, 3H, 3NH).
10b	3480-3360 (NH_2, 2NH), 3055 (CH. aromatic), 2975 (CH_3), 1680 (C=O), 1665 (exocyclic C=N), 1640 (C=C).	2.21 (s, 3H, CH_3), 5.33 (s, 2H, NH_2), 6.61 (s, 1H, thiazole H-5), 7.32-7.35 (m, 19H, aromatic-H), 8.43, 8.51 (2br s, 2H, 2NH).
11	3570-3380 (NH_2, 2NH), 3050 (CH. aromatic), 2940 (CH_3), 1680 (C=O), 1660 (exocyclic C=N), 1645 (C=C).	2.22 (s, 3H, CH_3), 5.38 (s, 2H, NH_2), 6.42 (s, 1H, thiazole H-5), 7.33-7.48 (m, 14H, aromatic-H), 8.22, 8.43 (2s, 2H, 2NH).

12a	3565-3390 (OH, NH_2, 2NH), 3060 (CH. aromatic), 2890 (CH_3), 1695 (C=O), 1670 (exocyclic C=N), 1640 (C=C).	2.23 (s, 3H, CH_3), 4.21 (s, 2H, NH_2), 6.66 (s, 1H, thiazole H-5), 7.33-7.46 (m, 14H, aromatic-H), 8.34, 8.45 (2s, 2H, 2NH), 10.30 (br s, 1H, OH).
12b	3570-3390 (OH, NH_2, 2NH), 3060 (CH. aromatic), 2975 (CH_3), 1670 (exocyclic C=N), 1645 (C=C), 1210-1195 (C=S).	
13a	3460-3370 (OH, 2NH), 3060 (CH. aromatic), 1670 (C=N), 1210-1200 (C=S).	6.99 (s, 1H, thiazole H-5), 7.40-7.48 (m, 10H, aromatic-H), 8.41, 8.46 (2s, 2H, 2NH), 10.29 (s, H, OH).
13b	3540-3350 (OH, 2NH), 3060 (CH. aromatic), 2890 (CH_3),1670 (C=N), 1210-1190 (C=S).	2.22 (s, 3H, CH_3), 6.99 (s, 1H, thiazole H-5), 7.31-7.44 (m, 9H, aromatic-H), 8.41, 8.44 (2s, 2H, 2NH), 10.31 (s, H, OH).
13c	3480-3320 (OH, 2NH), 3060 (CH. aromatic), 1670 (C=N), 1200-1190 (C=S).	6.99 (s, 1H, thiazole H-5), 7.32-7.48 (m, 9H, aromatic-H), 8.39, 8.42 (2s, 2H, 2NH).
13d	3570-3360 (OH, 2NH), 3060 (CH. aromatic), 2890 (CH_3), 1670 (C=N), 1205-1190 (C=S).	3.98 (s, 3H, CH_3), 6.87 (s, 1H, thiazole H-5), 7.0-7.05 (2d, 4H, C_6H_4), 7.21-7.40 (m, 5H, aromatic-H), 8.25, 8.44 (2s, 2H, 2NH), 10.25 (s, 1H, OH).
14	3540-3360 (2OH), 3065 (CH. aromatic), 2970 (CH_3), 1670 (2C=N), 1210-1190 (C=S).	2.23 (s, 3H, CH_3), 6.78, 6.89 (2s, 2H, two thiazole H-5), 7.33-7.45 (m, 9H, aromatic-H), 10.29, 10.35 (2s, 2H, 2OH).
15	3480-3335 (OH, 2NH), 3065 (CH. aromatic), 2983 (CH_3), 1670 (C=N), 1205-1190 (C=S).	2.28 (s, 3H, CH_3), 7.32-7.51 (m, 14H, aromatic-H), 8.29, 8.34 (2s, 2H, 2NH), 10.31 (s, H, OH).
16	3540-3370 (2NH), 3065 (CH. aromatic), 2970 (CH_3), 1690 (C=O), 1668 (exocyclic C=N), 1210-1190 (C=S).	2.23 (s, 3H, CH_3), 7.03 (s, 1H, CH=C), 7.32-7.46 (m, 14H, aromatic-H), 8.32, 8.46 (2br s, 2H, 2NH).
17a	3560-3350 (OH, 2NH), 2890 (CH_3), 2225, 2220 (CN), 1670 (C=N), 1640 (C=C).	2.25 (s, 3H, CH_3), 6.89 (s, 1H, thiazole H-5), 7.29-7.41 (m, 9H, aromatic-H), 8.23, 8.40 (2br s, 2H, 2NH), 10.29 (s, 1H, OH).
17b	3485-3325 (OH, 2NH), 3035 (CH. aromatic), 2975 (CH_3), 2220 (CN), 1680 (C=O), 1665 (exocyclic C=N), 1640 (C=C).	1.16 (t, 3H, CH_3), 2.28 (s, 3H, CH_3), 4.41 (q, 2H, CH_2), 6.89 (s, 1H, thiazole H-5), 7.21-7.42 (m, 9H, aromatic-H), 8.21, 8.37 (2br s, 2H, 2NH), 10.30 (s, 1H, OH).
19a	3540-3350 (OH, 2NH), 3065 (CH. aromatic), 2220 (CN), 1205-1190 (C=S).	7.32-7.48 (m, 10H, aromatic-H), 8.23, 8.41 (2s, 2H, 2NH), 10.25 (s, 1H, OH).
19b	3560-3365 (OH, 2NH), 3065 (CH. aromatic), 2965 (CH_3), 2220 (CN), 1670 (exocyclic C=N), 1205-1195 (C=S).	2.22 (s, 3H, CH_3), 7.32-7.41 (m, 9H, aromatic-H), 8.21, 8.42 (2s, 2H, 2NH), 10.35 (s, 1H, OH).
19c	3560-3325 (OH, 2NH), 3060 (CH. aromatic), 2220 (CN), 1670 (exocyclic C=N), 1205-1195 (C=S).	7.32-7.48 (m, 9H, aromatic-H), 8.32, 8.41 (2s, 2H, 2NH), 10.25 (s, 1H, OH).
19d	3575-3360 (OH, 2NH), 3060 (CH. aromatic), 2875 (CH_3), 2220 (CN), 1668 (exocyclic C=N), 1215-1195 (C=S).	3.90 (s, 3H, CH_3), 7.32-7.48 (m, 9H, aromatic-H), 8.23, 8.41 (2s, 2H, 2NH), 10.25 (s, 1H, OH).
20a	3560-3350 (OH, 2NH), 2980 (CH_3), 2230, 2225, 2220 (3CN), 1675 (exocyclic C=N), 1645 (C=C).	2.25 (s, 3H, CH_3), 7.29-7.41 (m, 9H, aromatic-H), 8.23, 8.40 (2s, 2H, 2NH), 10.30 (s, 1H, OH).
20b	3560-3350 (OH, 2NH), 2980 (CH_3), 2890 (CH_2), 2230, 2225, 2220 (3CN), 1675 (exocyclic C=N), 1645 (C=C).	1.16 (t, 3H, ester CH_3), 2.28 (s, 3H, CH_3), 4.41 (q, 2H, ester CH_2), 7.29-7.41 (m, 9H, aromatic-H), 8.21, 8.40 (2s, 2H, 2NH), 10.30 (s, 1H, OH).
22	3470-3360 (NH_2, 2NH), 2940 (CH_3), 1660 (exocyclic C=N), 1215-1195 (C=S).	2.20 (s, 3H, CH_3),5.32 (s, 2H, NH_2), 7.32-7.48 (m, 9H, aromatic-H), 8.22, 8.43 (2s, 2H, 2NH).
23a	3585-3360 ($2NH_2$, OH, 2NH), 2975 (CH_3), 2225 (CN), 1675 (exocyclic C=N), 1695 (C=O),1645 (C=C).	2.21 (s, 3H, CH_3), 4.51, 5.31 (2s, 4H, $2NH_2$), 7.32-7.41 (m, 9H, aromatic-H), 8.21, 8.42 (2s, 2H, 2NH), 10.30 (s, 1H, OH).
23b	3585-3360 ($2NH_2$, OH, 2NH), 2975 (CH_3), 2225 (CN), 1675 (exocyclic C=N), 1645 (C=C), 1210-1195 (C=S)	
23c	3560-3350 (NH_2, 2OH), 2975 (CH_3), 2225 (CN),1675 (exocyclic C=N), 1670 (C=O), 1645 (C=C).	2.21 (s, 3H, CH_3), 4.56 (s, 2H, NH_2), 7.32-7.41 (m, 9H, aromatic-H), 8.21, 8.42 (2s, 2H, 2NH), 10.10-10.30 (s, 2H, 2OH).
23d	3560-3350 (NH_2, 2OH), 2975 (CH_3), 2225 (CN),1675 (exocyclic C=N), 1645 (C=C), 1210-1195 (C=S).	
24a	3580-3360 ($3NH_2$, 3NH), 2970 (CH_3) 1675 (exocyclic C=N).	2.21 (s, 3H, CH_3), 4.51, 5.31, 5.35 (3s, 6H, $3NH_2$), 7.32-7.41 (m, 9H, aromatic-H), 8.21, 8.42 (3s, 3H, 3NH).
24b	3580-3300 (OH, $2NH_2$, 3NH), 2978 (CH_3) 1670 (exocyclic C=N).	2.21 (s, 3H, CH_3), 4.49, 5.33, (2s, 4H, $2NH_2$), 7.30-7.44 (m, 9H, aromatic-H), 8.21, 8.42, 9.01 (3s, 3H, 3NH).
24c	3560-3350 ($2NH_2$, 4NH), 2953 (CH_3), 1675 (exocyclic C=N), 1668 (C=O), 1645 (C=C).	2.21 (s, 3H, CH_3), 4.51, 5.32 (2s, 4H, $2NH_2$), 7.32-7.41 (m, 9H, aromatic-H), 8.21, 8.42 (4s, 4H, 4NH).
24d	3540-3300 ($2NH_2$, 3NH), 2950 (CH_3), 1666 (exocyclic C=N), 1680 (C=O), 1640 (C=C).	2.21 (s, 3H, CH_3), 4.51, 5.32 (2s, 4H, $2NH_2$), 7.32-7.41 (m, 19H, aromatic-H), 8.21, 8.42 (2br, 2s, 2H, 2NH).

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Key Words

Thiosemicarbazides; Thiazole; Pyrazole; Pyrimidines.

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