Some Reactions of 2- and 4-Substituted 8-Methylquinolin-2(1*H*)-ones and their Thio Analogues

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4-Amino-8-methyl-2-oxo/thioxoquinoline and 4-hydrazino-8-methyl-2-oxo/thioxoquinoline have been synthesized and used as synthons for the preparation of some new 4-substituted quinolin-2-ones and quinolinethiones. Also, 4-chloro-2-(ethoxycarbonylmethylthio)-8-methylquinoline was synthesized and utilized as a precursor for some new triazoles, thiadiazoles, benzimidazoles, benzthiazoles, and oxadiazoles bearing the quinoline moiety at position 2.

The biological importance of quinolinones [1—4] stimulated an intensive research work for the synthesis of many members of this class of compounds. Within the framework of research related to the chemistry of substituted quinolinones [5—9], the synthesis and properties of some new quinolinones and quinolinethiones substituted at positions 4 and 2 are reported.

4-Chloro/amino/hydrazino-8-methylquinolin-2-ones *Ia*—*IIIa* and their analogues *Ib*—*IIIb* [10, 11] were synthesized (Scheme 1) and used as synthons for some novel heterocyclic moieties as substituents to quinolinone or quinolinethione, which may have promising biological activity.

On the other hand, 4-chloro-2-(ethoxycarbonylmethylthio)-8-methylquinoline (*IV*) was also synthesized aiming to prepare some new 2-heterocyclic substituted methylthioquinoline derivatives, which are of expected considerable biological activity. *S*-Alkylation of compound *Ib* was carried out using ethyl chloroacetate in the presence of base catalysts to give the required *IV*.

Reaction of 4-amino-8-methyl-2-oxo/thioxoquinolines (*IIa, IIb*) with phenyl isothiocyanate (Scheme 2) in ethanol gave *N*-(8-methyl-2(1*H*)-oxo/thioxoquinolin-4-yl)-*N*′-phenylthiourea (*Va, Vb*). On the other hand, condensation reaction of the aminoquinolines *IIa, IIb* with isatin in DMF gave the corresponding imine products *VIa, VIb*. Similarly, treatment of *IIa, IIb* with 3-formyl-4-hydroxy-8-methylquinolin-2(1*H*)-one (*VII*) led to interesting Schiff bases *VIIIa, VIIIb*.

For the purpose of obtaining various 4-substituted 2-oxo/thioxoquinolines, 4-hydrazino-8-methyl-2-oxo/thioxoquinolines (*IIIa, IIIb*) were subjected to react with some selected reagents. Thus, *IIIa, IIIb* were reacted with phenyl isothiocyanate in boiling DMF to give the corresponding quinolinylthiosemicarbazides *IXa, IXb* (Scheme 3). IR and ^{1}H NMR spectra elucidated their structure revealing the existence of NHC═S group. The tendency of the hydrazinoquinolinones *IIIa,* or their thio analogues *IIIb* towards addition-elimination reactions was also investigated. Thus, the reaction of *IIIa, IIIb* with *p*-toluenesulfonyl chloride in dry pyridine furnished 4-tosylhydrazino derivatives *Xa, Xb* the structure of which was elucidated by elemental analysis, IR, and ^{1}H NMR spectral data. IR spectrum revealed the presence of two peaks at $\tilde{\nu}$ = 1350 and 1160 cm^{-1} due to S═O sulfone hydrazide. On the other hand, the condensation reaction of the hydrazino compounds *IIIa, IIIb* with aldehyde *VII* in dioxane led to interesting hydrazones *XIa, XIb*.

Surprisingly, during trials to purify the materials *XIa, XIb* by crystallization from hot glacial acetic acid, the output products *XIIa, XIIb* were found having properties very different from the precrystallized materials. The resultants 6-methyl-1-(8-methyl-2(1*H*)-oxo/thioxoquinolin-4-yl)-4,5-dihydro-1*H*-pyrazolo[4,3-*c*]-quinolin-4(5*H*)-ones (*XIIa, XIIb*) gave a negative ferric chloride test for phenolic —OH group, indicating with no doubt that both phenolic —OH and —NH groups are absent due to their involvement in an intramolecular cyclization reaction with exclusion of a water molecule to form pyrazole ring. Moreover, compounds *XIIa, XIIb* were also obtained when the hydrazino compounds *IIIa, IIIb* were subjected to react with the same aldehyde in glacial acetic acid and fused sodium acetate.

The ester *IV* was subjected to react with *o*-

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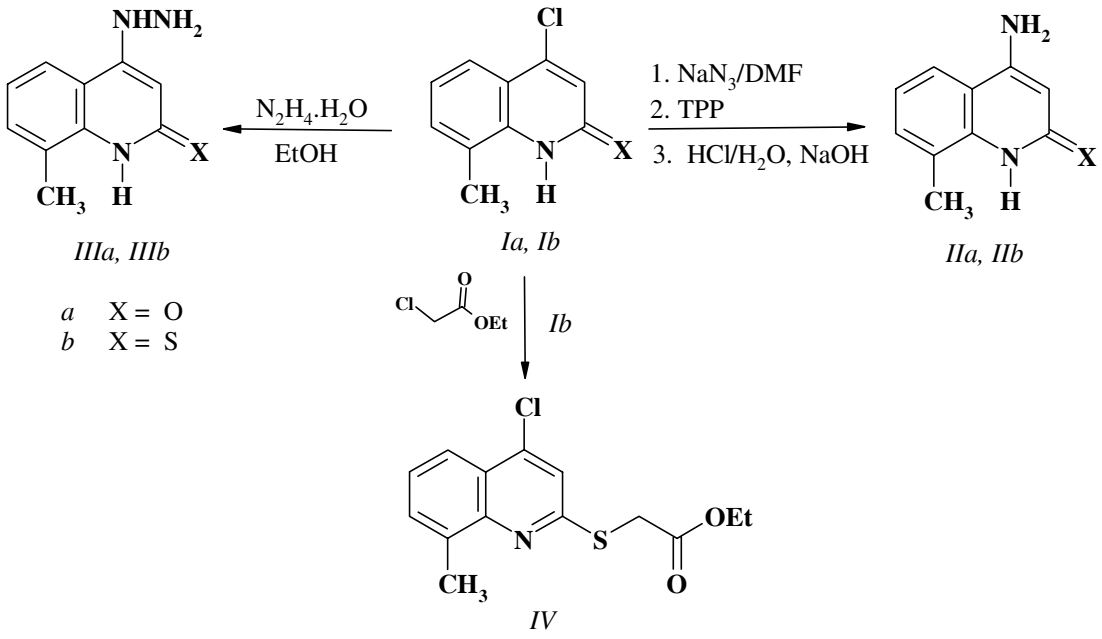
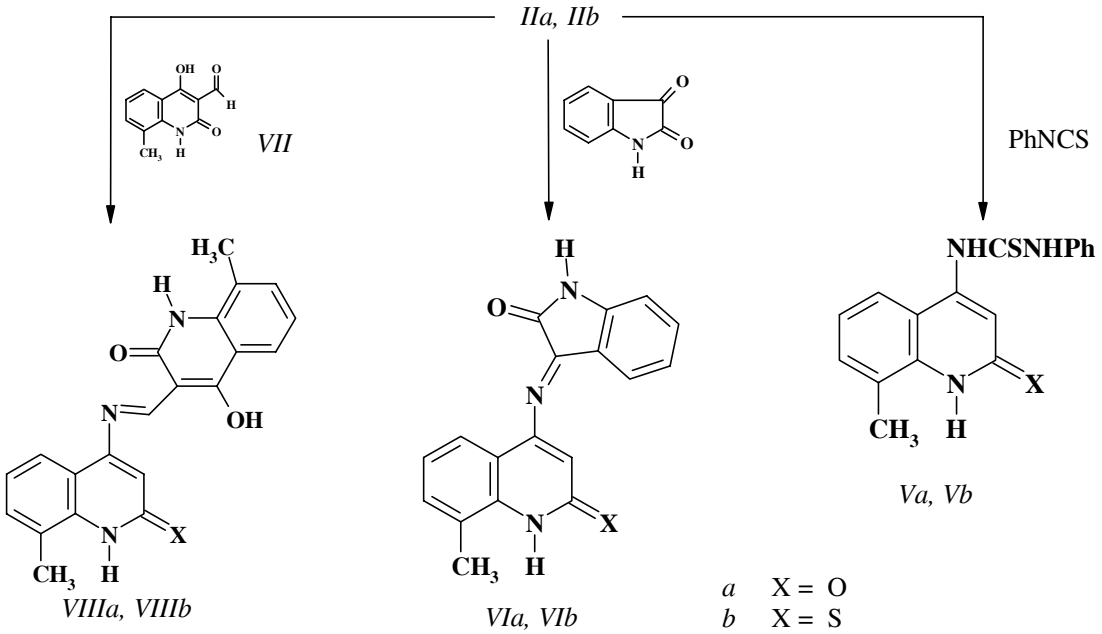
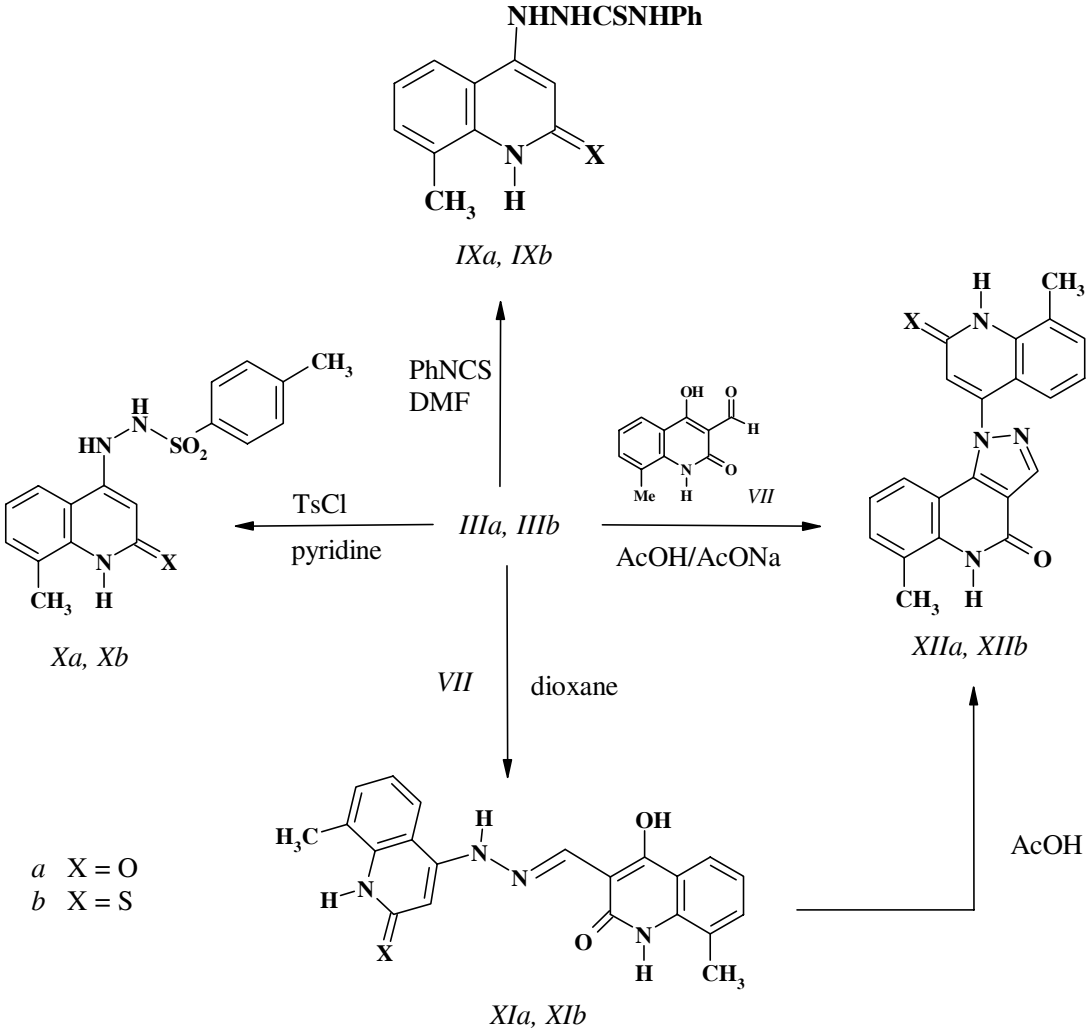


Scheme 1



Scheme 2

phenylenediamine or *o*-aminothiophenol giving 2-(benzimidazol-2-ylmethylthio)- (*XIIIa*) and 2-(benzothiazol-2-ylmethylthio)-4-chloro-8-methylquinoline (*XIIIb*), respectively (Scheme 4). The structures of both compounds *XIIIa* and *XIIIb* were derived from elemental microanalyses. Also, IR spectra showed the disappearance of the vibrational bands corresponding to the ester group. As it was mentioned here before the synthesis of heterocyclic substituted methylthioquinolines was aimed, so that it was planned to prepare an acid hydrazide, which might serve as a good precursor for obtaining those new systems. Thus, the reaction of the ester *IV* with hydrazine hydrate in ethanol at room temperature gave the corresponding acid hydrazide *XIV* (in 55 % yield). The trials to improve the yield of compound *XIV via* heating the ester *IV* with excess hydrazine hydrate without solvent caused unexpected nucleophilic hydrazinolysis at positions 2 and 4, affording 2,4-dihydrazino-8-methylquinoline *XV*. Similar observation was reported in our previous publication [11]. The structure of the dihydrazinoquinoline *XV* was also established by its reaction with nitrous acid which led to 5-azido-8-methyltetrazolo[1,5-*a*]quinoline *XVI* [11].



Scheme 3

Reaction of the acid hydrazide *XIV* with nitrous acid furnished an acetylazide derivative *XVII*. Interpretation of the IR spectral data of the latter product supported the proposed structure, where an absorption band specific for the azido group appeared at 2115 cm^{-1}.

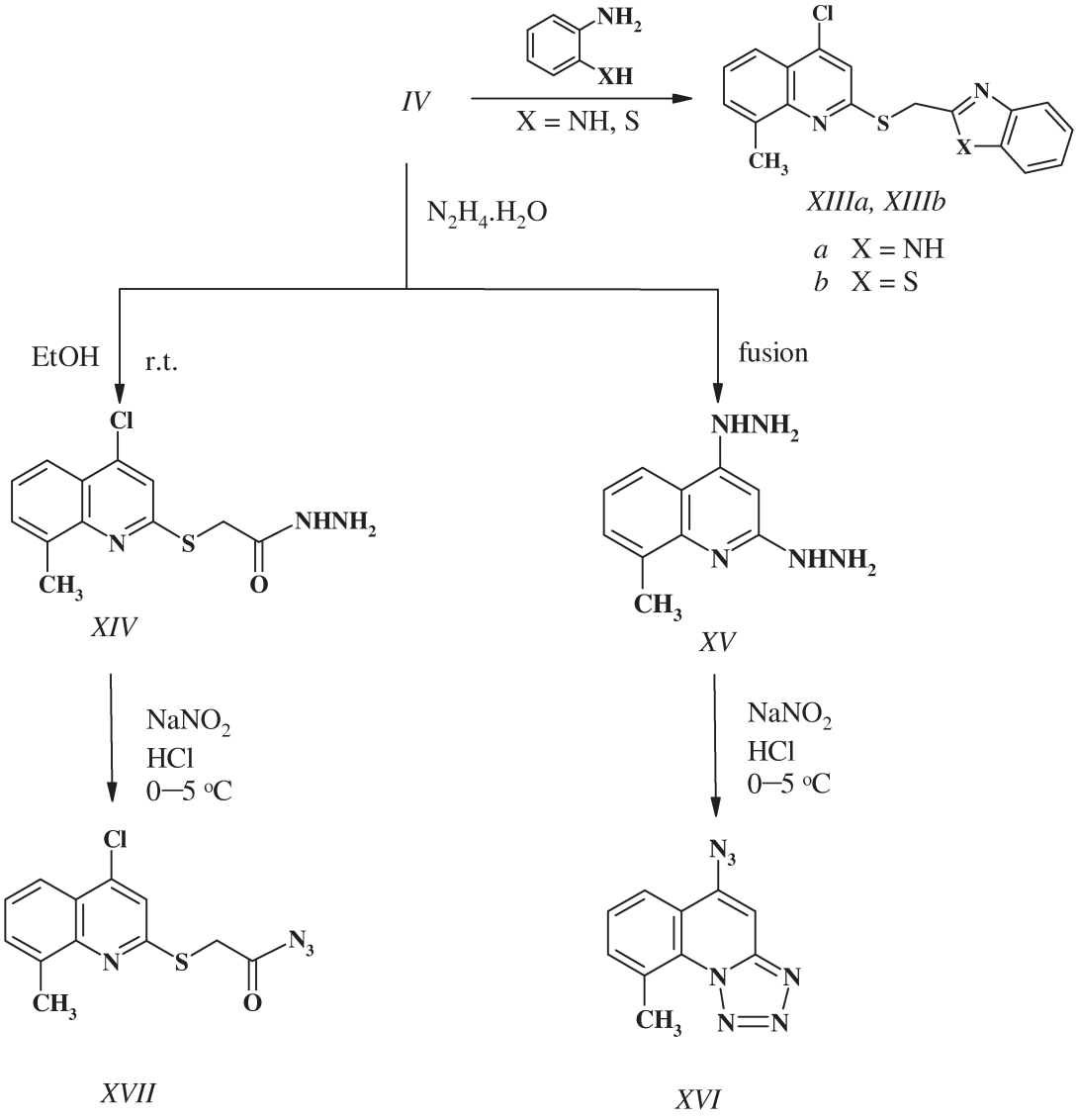
Treatment of the acid hydrazide *XIV* with phenyl isothiocyanate in boiling ethanol afforded the corresponding thiosemicarbazide derivative *XVIII* (Scheme 5). When the latter compound was treated with alcoholic potassium hydroxide, cyclization reaction took place in which the carbonylthiosemicarbazide side chain underwent intramolecular cyclocondensation to give 4-chloro-8-methyl-2-(3-sulfanyl-4-phenyl-4*H*-1,2,4-triazol-5-ylmethylthio)quinoline (*XIX*) [12], the IR and ^{1}H NMR spectra of which showed that it exists essentially as Δ^2-1,2,4-triazoline-3-thione form.

On the other hand, treatment of the compound *XVIII* with polyphosphoric acid (PPA) furnished cyclization of the carbonylthiosemicarbazide side chain; the elemental analysis of the product of the latter reaction proved the loss of a molecule of water during the cyclization as well as in the previous reaction. From the integration of both analytical and spectral data it is deduced that the product of the latter reaction may be 4-chloro-8-methyl-2-(2-phenylimino-1,3,4-thiadiazol-5-ylmethylthio)quinoline (*XX*).

For obtaining other five-membered heterocyclic substituted methylthioquinolines, the reaction of the acid hydrazide *XIV* with carbon disulfide in the presence of alcoholic potassium hydroxide afforded 4-chloro-8-methyl-2-(2-sulfanyl-1,3,4-oxadiazol-5-ylmethylthio)quinoline (*XXII*), which may be thought to be the product of cyclization of a not separated intermediate potassium dithiocarbazate *XXI*.

Methylation of the oxadiazole *XXII* using methyl iodide in the presence of aqueous potassium hydroxide led to the formation of 4-chloro-8-methyl-2-(2-methylthio-1,3,4-oxadiazol-5-ylmethylthio)quinoline (*XXIII*).

Finally, the reaction of the acid hydrazide *XIV* with carbon disulfide and hydrazine hydrate in the presence of alcoholic potassium hydroxide [13] furnished 2-(4-amino-3-sulfanyl-4*H*-1,2,4-triazol-5-ylme-



Scheme 4

thylthio)-4-chloro-8-methylquinoline (*XXIV*). The structure of the latter compound was emphasized on the basis of its correct C, H, N elemental analysis, solubility in both acids and bases, and also IR and ^{1}H NMR spectral data. IR spectrum indicated the presence of sulfanyl group —SH absorption band at $\tilde{\nu}$ = 2730 cm^{-1} and bands at 3340, 3430 cm^{-1} specific for —NH_2 group. ^{1}H NMR spectrum of *XXIV* showed signal at δ = 2.10 specific for —SH group and another broad signal at δ = 6.20 due to —NH_2.

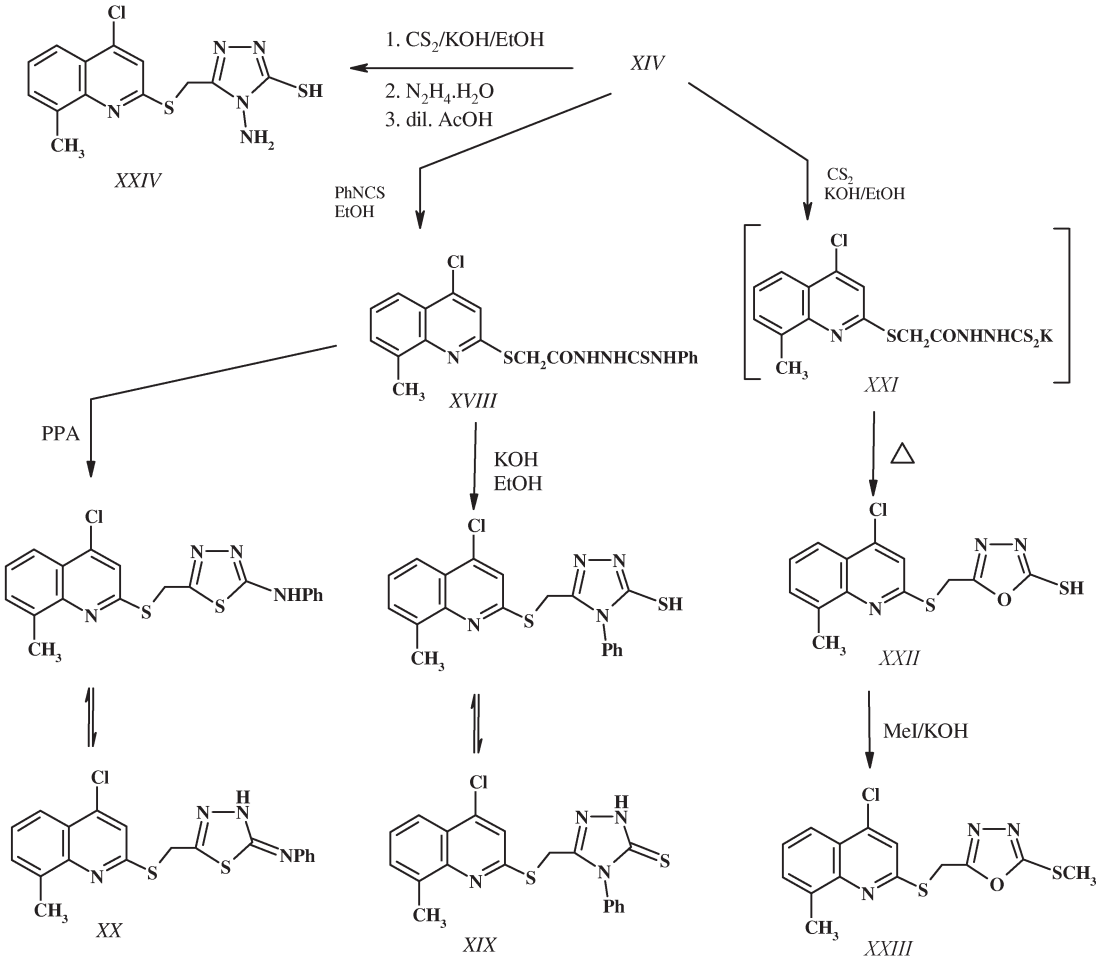
EXPERIMENTAL

Melting points are uncorrected and were determined in open capillary tubes on Gallenkamp MFB-595 apparatus. IR spectra were taken on a Perkin—Elmer FT-IR 1650 spectrophotometer, using samples in KBr discs. ^{1}H NMR spectra were measured on Jeol FX-90 spectrometer at 90 MHz, using DMSO-d_6 as solvent and TMS as internal standard. Elemental analyses were performed on a Perkin—Elmer CHN-2400 analyzer. The syntheses of compounds *I—III, VII, XV, XVI* were previously described [9—11]. Analytical and spectral data are listed in Tables 1 and 2.

4-Chloro-2-(ethoxycarbonylmethylthio)-8-methylquinoline (*IV*)

A mixture of *Ib* (0.01 mol), ethyl chloroacetate (0.015 mol), and anhydrous potassium carbonate (15 g) in dry dioxane (100 cm^3) was refluxed on a water bath for 24 h. The reaction mixture was allowed to cool and then it was poured into water. The resultant solid so formed was filtered off, dried and crystallized.

N-(8-Methyl-2(1*H*)-oxo/thioxoquinolin-4-yl)-*N*′-phenylthiourea (*Va, Vb*)



Scheme 5

A mixture of compound *IIa* or *IIb* (0.01 mol) and phenyl isothiocyanate (0.011 mol) in ethanol (20 cm^3) was refluxed for 3 h. The solid so formed was filtered off, washed with ethanol (20 cm^3) and crystallized.

3-(8-Methyl-2(1*H*)-oxo/thioxoquinolin-4-ylimino)indolin-2-one (*VIa, VIb*)

Equimolar amounts (0.01 mol) of *IIa* or *IIb* and isatin in boiling DMF (25 cm^3) were heated under reflux for 3 h. The deposits, which formed on hot, were filtered off and crystallized.

3-(8-Methyl-2(1*H*)-oxo/thioxoquinolin-4-yliminomethyl)-4-hydroxy-8-methylquinolin-2(1*H*)-one (*VIIIa, VIIIb*)

A mixture of the aminoquinoline *IIa* or *IIb* (0.01 mol) and the aldehyde *VII* (0.01 mol) in DMF (25 cm^3) was refluxed for 1 h. The solid product so obtained during the course of the reaction was filtered off and crystallized.

1-(8-Methyl-2(1*H*)-oxo/thioxoquinolin-4-yl)-4-phenylthiosemicarbazide (*IXa, IXb*)

A mixture of *IIIa* or *IIIb* (0.01 mol) and phenyl isothiocyanate (0.01 mol) in DMF (20 cm^3) was refluxed for 2 h. The precipitate so obtained during the course of the reaction was collected by filtration and crystallized.

8-Methyl-4-tosylhydrazino-2(1*H*)-oxo/thioxoquinoline (*Xa, Xb*)

A mixture of *IIIa* or *IIIb* (0.01 mol) and *p*-toluenesulfonyl chloride (0.01 mol) in dry pyridine (20 cm^3) was stirred at 70—80 °C for 2 h and then diluted with ice-cold water containing hydrochloric acid. The resulting precipitate was collected by filtration and crystallized.

4-Hydroxy-8-methyl-2(1*H*)-oxoquinoline-3-carbaldehyde (8-Methyl-2(1*H*)-oxo/thioxoquinolin-4-yl)hydrazone (*XIa, XIb*)

Table 1. Analytical Data of the New Compounds

Compound	Formula M_r	w_i(calc.)/% w_i(found)/% C	H	N	Yield %	M.p./°C Solvent
IV	$C_{14}H_{14}NO_2SCl$	56.85	4.74	4.74	63	99—100
	295.5	56.80	4.70	4.70		Acetone
Va	$C_{17}H_{15}N_3OS$	66.02	4.85	13.59	80	> 300
	309	66.00	4.90	13.50		EtOH
Vb	$C_{17}H_{15}N_3S_2$	62.77	4.62	12.92	75	> 300
	325	62.50	4.60	13.00		DMF
VIa	$C_{18}H_{13}N_3O_2$	71.29	4.29	13.86	76	> 300
	303	71.30	4.30	13.90		EtOH/H_2O
VIb	$C_{18}H_{13}N_3OS$	67.71	4.08	13.17	73	> 300
	319	68.00	4.00	13.20		DMF
VIIIa	$C_{21}H_{17}N_3O_3$	70.19	4.74	11.70	75	> 300
	359	70.20	4.70	11.70		DMF
VIIIb	$C_{21}H_{17}N_3O_2S$	67.20	4.53	11.20	88	> 300
	375	67.00	4.30	11.00		EtOH
IXa	$C_{17}H_{16}N_4OS$	62.96	4.94	17.28	84	244—245
	324	63.10	4.80	17.10		DMF
IXb	$C_{17}H_{16}N_4S_2$	60.00	4.71	16.47	85	152—154
	340	60.10	4.60	16.20		EtOH
Xa	$C_{17}H_{17}N_3O_3S$	59.48	4.96	12.24	86	210—212
	343	59.20	4.90	12.20		Dioxane
Xb	$C_{17}H_{17}N_3O_2S_2$	56.82	4.74	11.70	66	199—200
	359	56.60	4.50	11.40		EtOH
XIa	$C_{21}H_{18}N_4O_3$	67.38	4.81	14.97	78	> 300
	374	67.20	4.60	14.80		DMF
XIb	$C_{21}H_{18}N_4O_2S$	64.62	4.62	14.36	75	>300
	390	64.50	4.30	14.30		DMF
XIIa	$C_{21}H_{16}N_4O_2$	70.79	4.49	15.73	90	> 300
	356	70.70	4.40	15.50		AcOH
XIIb	$C_{21}H_{16}N_4OS$	67.74	4.30	15.05	83	> 300
	372	67.60	4.20	14.80		AcOH
XIIIa	$C_{18}H_{14}N_3SCl$	63.62	4.12	12.37	55	244—246
	339.5	63.40	4.10	12.20		EtOH
XIIIb	$C_{18}H_{13}N_2S_2Cl$	60.59	3.65	7.85	64	230—232
	356.5	60.30	3.40	7.50		Dioxane
XIV	$C_{12}H_{12}N_3OSCl$	51.15	4.26	14.92	55	180—182
	281.5	51.20	4.20	15.00		Benzene
XVII	$C_{12}H_9N_4OSCl$	49.23	3.08	19.15	72	104—106
	292.5	49.20	3.00	18.80		EtOH
XVIII	$C_{19}H_{17}N_4OS_2Cl$	54.74	4.08	13.45	85	148—150
	416.5	54.50	3.90	13.30		MeOH
XIX	$C_{19}H_{15}N_4S_2Cl$	57.21	3.76	14.05	64	140—142
	398.5	57.10	3.70	13.90		EtOH
XX	$C_{19}H_{15}N_4S_2Cl$	57.21	3.76	14.05	57	163—165
	398.5	57.20	3.60	13.80		EtOH
XXII	$C_{13}H_{10}N_3OS_2Cl$	48.22	3.09	12.98	75	122—124
	323.5	48.20	3.00	12.80		EtOH
XXIII	$C_{14}H_{12}N_3OS_2Cl$	49.78	3.56	12.44	83	88—90
	337.5	49.60	3.50	12.20		MeOH
XXIV	$C_{13}H_{12}N_5S_2Cl$	46.22	3.56	20.74	70	178—180
	337.5	46.10	3.40	20.50		Dioxane

A mixture of *IIIa* or *IIIb* (0.01 mol) and 3-formyl derivative *VII* (0.01 mol) in dioxane was refluxed for 4 h. The product so formed during the course of the reaction was filtered off and crystallized.

6-Methyl-1-(8-methyl-2(1*H*)-oxo/thioxo-quinolin-4-yl)-4,5-dihydro-1*H*-pyrazolo[4,3-*c*]quinolin-4(5*H*)-ones (*XIIa, XIIb*)

Table 2. Spectral Data of the New Compounds

Compound	IR, $\tilde{\nu}$/cm^{-1}	^{1}H NMR, δ
IV	750 ν(C—Cl), 1120 ν(C—O—C), 1615 ν(C═N), 1735 ν(C═O$_{ester}$), 2860—2990 ν(CH$_{aliph}$), 3080 ν(CH$_{arom}$)	1.20 (t, 3H, CH$_3$CH$_2$O), 2.60 (s, 3H, CH$_3$-8), 3.50 (s, 2H, SCH$_2$CO), 4.20 (q, 2H, CH$_3$CH$_2$O), 6.90 (s, 1H, H-3$_{quinoline}$), 7.25—8.05 (m, 3H, H$_{arom}$)
Va	1310, 1250, 1025 ν(NHC═S), 1660 ν(C═O), 2980 ν(CH$_{aliph}$), 3040 ν(CH$_{arom}$), 3280—3360 ν(N—H)	2.35 (s, 3H, CH$_3$), 5.95 (s, 1H, H-3$_{quinoline}$), 7.15—8.00 (m, 8H, H$_{arom}$), 9.35—9.85 (b, 2H, 2 × N—H$_{thiourea}$), 10.40 (bs, 1H, N—H$_{quinolinone}$)
Vb	1320, 1250, 1035 ν(NHC═S), 1663 ν(C═O), 2950—2995 ν(CH$_{aliph}$), 3060—3090 ν(CH$_{arom}$), 3275—3355 ν(N—H)	
VIa	1620 ν(C═N), 1645, 1670 ν(C═O), 2950 ν(CH$_{aliph}$), 3040—3080 ν(CH$_{arom}$), 3120—3220 ν(N—H$_{lactam}$)	2.38 (s, 3H, CH$_3$), 6.8 (s, 1H, H-3$_{quinolinone}$), 7.10—7.95 (m, 7H, H$_{arom}$), 10.40 (bs, 1H, N—H$_{quinolinone}$), 11.35 (bs, 1H, N—H$_{indolone}$)
VIb	1610 ν(C═N), 1650, 1665 ν(C═O), 2970—2985 ν(CH$_{aliph}$), 3090 ν(CH$_{arom}$), 3130—3220 ν(N═H$_{lactam}$)	
VIIIa	1615 ν(C═N), 1645, 1660 ν(C═O$_{quinolinone}$), 3210, 2611—3191 ν(N—H, H-bonded OH)	2.30 (s, 3H, CH$_3$), 2.60 (s, 3H, CH$_3$), 6.35 (s, 1H, H-3$_{quinolinone}$), 7.10—8.05 (m, 6H, H$_{arom}$), 8.45 (s, 1H, H—C═N), 10.40—10.55 (bs, 2H, 2 × NH), 11.80 (bs, 1H, O—H)
VIIIb	1325, 1270, 1072 ν(NHC═S), 1620 ν(C═N), 1645 ν(C═O), 2660 ν(b, H-bonded OH), 3110—3120 ν(N—H)	2.50—2.60 (two s, 6H, 2 × CH$_3$), 6.35 (s, 1H, H-3$_{quinoline}$), 7.05—8.10 (m, 6H, H$_{arom}$), 8.55 (s, 1H, H—C═N), 10.45 (s, 1H, CSN—H), 10.65 (s, 1H, CON—H), 11.80 (s, 1H, O—H)
IXa	1340, 1275, 1060 ν(NHC═S), 1615 ν(C═N), 1650 ν(C═O), 2825—3200 ν(b, NH, S—H)	2.30 (s, 3H, CH$_3$), 5.85 (s, 1H, H-3$_{quinoline}$), 7.10—8.05 (m, 8H, H$_{arom}$), 8.70 (bs, N-1—H$_{thiosemicarbazide}$), 9.85—9.90 (b, 2H, N-2—H and N-4—H$_{thiosemicarbazide}$), 10.42 (bs, 1H, N—H$_{quinoline}$)
IXb	1350, 1235, 1165 ν(NHC═S), 2820—3230 ν(b, N—H and S—H)	1.80 (bs, 0.3H, tautomeric S—H), 2.35 (s, 3H, CH$_3$), 6.35 (s, 1H, H-3$_{quinoline}$), 7.05—8.15 (m, 8H, H$_{arom}$), 8.35 (bs, 1H, N-1—H$_{thiosemicarbazide}$), 9.30—9.45 (b, 2H, N-2—H and N-4—H$_{thiosemicarbazide}$), 10.40 (bs, 0.7H, N—H$_{quinoline}$)
Xa	1160, 1355 ν(S═O), 1655 ν(C═O), 2120—3260 ν(N—H)	1.96 (s, 3H, CH$_3$), 2.40 (s, 3H, CH$_3$), 5.85 (s, 1H, H-3$_{quinoline}$), 7.25—8.15 (m, 7H, H$_{arom}$), 9.30 (s, 1H, SO$_2$NHNHR), 9.65 (s, 1H, SO$_2$NHNHR), 10.35 (s, 1H, N—H$_{lactam}$)
Xb	1160, 1350 ν(S═O$_{sulfohydrazide}$), 2720 ν(H-bonded SH), 3175—3210 ν(N—H)	1.80 (bs, 0.4H, tautomeric SH), 2.30 (s, 3H, CH$_3$), 2.45 (s, 3H, CH$_3$), 5.85 (s, 1H, H-3$_{quinoline}$), 6.95—8.05 (m, 7H, H$_{arom}$), 8.45 (s, 1H, N—H$_{hydrazide}$), 10.30 (s, 0.6 H, tautomeric N—H$_{quinoline}$), 10.85 (s, 1H, SO$_2$N-1—H)
XIa	1612 ν(C═N), 1645 ν(C═O), 1660 ν(C═O), 2660 ν(H-bonded OH), 3160—3210 ν(N—H)	1.95 (s, 3H, CH$_3$), 2.25 (s, 3H, CH$_3$), 5.85 (s, 1H, H-3$_{quinoline}$), 7.10—8.05 (m, 6H, H$_{arom}$), 8.30 (s, 1H, CH═N), 9.80 (s, 1H, C═N—N—H), 10.60 (s, 1H, N—H$_{lactam}$), 10.80 (s, 1H, O—H)
XIb	1240, 1145, 1080 ν(NHC═S), 1610 ν(C═N), 1645 ν(C═O), 2550—3170 ν(b, N—H and H-bonded OH)	1.65 (bs, 0.2H, tautomeric SH), 2.60, 2.65 (two s, 6H, 2 × CH$_3$), 6.80 (s, 1H, H-3$_{quinoline}$), 7.05—8.10 (m, 6H, H$_{arom}$), 8.25 (s, 1H, N—H), 8.45 (s, 1H, CH═N), 10.40 (b, 0.8H, tautomeric CSN—H), 10.65 (s, 1H, CON—H), 11.60 (s, 1H, O—H)
XIIa	1620 ν(C═N), 1640 ν(C═O), 1660 ν(C═O), 3120 ν(N—H)	2.20 (s, 3H, CH$_3$), 2.55 (s, 3H, CH$_3$), 6.15 (s, 1H, H-3$_{quinoline}$), 7.15—8.10 (m, 7H, H$_{arom}$ + H-3$_{pyrazole}$), 10.50 (s, 1H, N—H$_{lactam}$), 10.75 (s, 1H, N—H$_{lactam}$)
XIIb	1035, 1190, 1240 ν(NHC═S), 1615 ν(C═N), 1645 ν(C═O), 2880 ν(S—H), 3165 ν(N—H)	1.65 (s, 0.3H, tautomeric SH), 2.20 and 2.40 (two s, 6H, 2 × CH$_3$), 6.35 (s, 1H, H-3$_{quinoline}$), 7.10—8.05 (m, 7H, H$_{arom}$ + H-3$_{pyrazole}$), 10.40 (b, 0.7H, tautomeric CSN—H), 10.65 (s, 1H, CON—H)
XIIIa	750 ν(C—Cl), 1600—1610 ν(C═N), 3160 ν(N—H)	
XIIIb	752 ν(C—Cl), 1605—1620 ν(C═N), 2960 ν(CH$_{aliph}$), 3070 ν(CH$_{arom}$)	2.35 (s, 3H, CH$_3$), 3.40 (s, 2H, SCH$_2$—), 6.85 (s, 1H, H-3$_{quinoline}$), 7.15—8.05 (m, 7H, H$_{arom}$)

Table 2 (Continued)

Compound	IR, $\tilde{\nu}$/cm^{-1}	^{1}H NMR, δ
XIV	752 ν(C—Cl), 1620 ν(C═N), 1685 ν(C═O$_{\text{acid hydrazide}}$), 3170 ν(N—H), 3350—3430 ν(NH$_2$)	2.10 (s, 3H, CH$_3$), 3.25 (s, 2H, SCH$_2$—), 5.85 (s, 1H, H-3$_{\text{quinoline}}$), 6.40 (bs, 2H, NH$_2$), 6.95—7.90 (m, 3H, H$_{\text{arom}}$), 9.85 (bs, 1H, CON—H)
XVII	1725 ν(C═O), 2115, 2220 ν(CON$_3$), 2960 ν(CH$_{\text{aliph}}$), 3070 ν(CH$_{\text{arom}}$)	2.35 (s, 3H, CH$_3$), 3.40 (s, 2H, SCH$_2$CON$_3$), 6.80 (s, 1H, H-3$_{\text{quinoline}}$), 7.25—8.10 (m, 3H, H$_{\text{arom}}$)
XVIII	1060, 1125, 1245 ν(NHC═S), 1620 ν(C═N), 1705 ν(C═O), 3120—3180 ν(N—H)	2.10 (s, 3H, CH$_3$), 3.40 (s, 2H, SCH$_2$—), 6.35 (s, 1H, H-3$_{\text{quinoline}}$), 6.95—7.90 (m, 8H, H$_{\text{arom}}$), 8.85 (bs, 1H, N—H), 9.35 (bs, 1H, N—H), 9.80 (bs, 1H, N—H)
XIX	750 ν(C—Cl), 1070, 1145, 1272 ν(NHC═S), 1610—1620 ν(C═N), 2975 ν(CH$_{\text{aliph}}$), 3030—3065 ν(CH$_{\text{arom}}$)	2.32 (s, 3H, CH$_3$), 3.45 (s, 2H, SCH$_2$—), 5.95 (s, 1H, H-3$_{\text{quinoline}}$), 7.15—8.10 (m, 8H, H$_{\text{arom}}$), 9.95 (bs, 1H, CSN—H)
XX	752 ν(C—Cl), 1018, 1206 ν(C—S—C), 1605—1620 ν(C═N), 3140—3172 ν(N—H)	2.10 (s, 3H, CH$_3$), 3.40 (s, 2H, SCH$_2$—), 6.30 (s, 1H, H-3$_{\text{quinoline}}$), 7.05—7.95 (m, 8H, H$_{\text{arom}}$), 8.85 (s, 1H, N—H)
XXII	750 ν(C—Cl), 1100 ν(C—O—C), 1610—1630 ν(C═N), 2660 ν(b, S—H)	2.15 (s, 3H, CH$_3$), 2.40 (bs, 1H, S—H), 3.30 (s, 2H, SCH$_2$—), 6.65 (s, 1H, H-3$_{\text{quinoline}}$), 7.15—8.05 (m, 3H, H$_{\text{arom}}$)
XXIII	1110, 1200 ν(C—O—C, C—S—C), 1605—1625 ν(C═N), 2940—2970 ν(CH$_{\text{aliph}}$), 3070 ν(CH$_{\text{arom}}$)	2.20 (s, 3H, CH$_3$), 2.95 (s, 3H, SCH$_3$), 3.30 (s, 2H, SCH$_2$—), 6.15 (s, 1H, H-3$_{\text{quinoline}}$), 7.20—8.05 (m, 3H, H$_{\text{arom}}$)
XXIV	1600—1630 ν(C═N), 2730 ν(S—H), 3340, 3430 ν(NH$_2$)	2.10 (s, 1H, SH), 2.25 (s, 3H, CH$_3$-8), 3.30 (s, 2H, SCH$_2$—), 6.20 (bs, 2H, 3NH$_2$), 6.65 (s, 1H, H-3$_{\text{quinoline}}$), 7.25—8.05 (m, 3H, H$_{\text{arom}}$)

Method A. To a solution of compound *IIa* or *IIb* (0.01 mol) in glacial acetic acid (20 cm^3) few drops of acetic anhydride were added. The reaction mixture was refluxed for 6 h. The precipitate so formed was filtered off and crystallized.

Method B. A mixture of equimolar amounts (0.01 mol) of *IIIa* or *IIIb* and *VII* was treated with acetic acid (25 cm^3) and fused sodium acetate (0.01 mol). The mixture was then heated under reflux for 5 h. The reaction mixture was poured into ice-cold water (50 cm^3) and the precipitate so obtained was filtered off and crystallized.

2-(Benzimidazol-2-ylmethylthio)- (*XIIIa*) and 2-(Benzothiazol-2-ylmethylthio)-4-chloro-8-methylquinoline (*XIIIb*)

A mixture of compound *IV* (0.01 mol) and *o*-phenylenediamine or *o*-aminothiophenol was heated under fusion conditions in the presence of PPA for 2 h. The mass of the reaction was allowed to cool and it was poured into cold water containing sodium acetate (20 g). The solid so formed was filtered off and crystallized.

(4-Chloro-8-methylquinolin-2-yl)thioacetylhydrazide (*XIV*)

To a solution of compound *IV* (0.01 mol) in absolute ethanol (30 cm^3) hydrazine hydrate (0.01 mol) was added and the reaction mixture was left at room temperature overnight. The solid so formed was collected by filtration and crystallized.

(4-Chloro-8-methylquinolin-2-yl)thioacetylazide (*XVII*)

To a solution of *XIV* (0.01 mol) in 2 M-hydrochloric acid (5 cm^3) sodium nitrite solution (5 g in 100 cm^3 of water) was dropwise added with continuous stirring in crushed ice. The precipitate so formed was collected and crystallized.

1-(4-Chloro-8-methylquinolin-2-ylthioacetyl)-4-phenylthiosemicarbazide (*XVIII*)

A mixture of *XIV* (0.01 mol) and phenyl isothiocyanate (0.01 mol) in absolute ethanol (30 cm^3) was refluxed for 4 h. The mixture was poured into ice-cold water, afterwards the precipitate so formed was filtered off and crystallized.

4-Chloro-8-methyl-2-(3-sulfanyl-4-phenyl-4*H*-1,2,4-triazol-5-ylmethylthio)quinoline (*XIX*)

To a solution of compound *XVIII* (0.01 mol) in ethanol (30 cm^3, 95 %) potassium hydroxide (0.015 mol) was added. The reaction mixture was heated under reflux for 4 h. The mixture was then filtered and acidified with diluted hydrochloric acid. The precipitate that separated was collected by filtration and crystallized.

4-Chloro-8-methyl-2-(2-phenylimino-1,3,4-thiadiazol-5-ylmethylthio)quinoline (*XX*)

Using the same method as for preparation of *XIIIa,*

treatment of compound *XVIII* with PPA yielded *XX*.

4-Chloro-8-methyl-2-(2-sulfanyl-1,3,4-oxadiazol-5-ylmethylthio)quinoline (*XXII*)

To a solution of potassium hydroxide (0.15 mol) in absolute ethanol (100 cm^3) compound *XIV* (0.01 mol) was added and then treated with carbon disulfide (0.02 mol). The reaction mixture was refluxed for 4 h, then the mass of the reaction after cooling was poured into ice-cold water, acidified with diluted hydrochloric acid and the solid so separated was collected and crystallized.

4-Chloro-8-methyl-2-(2-methylthio-1,3,4-oxadiazol-5-ylmethylthio)quinoline (*XXIII*)

A solution of compound *XXII* (0.01 mol) in aqueous solution of 1 M-potassium hydroxide (20 cm^3) was treated with equimolar amount of methyl iodide. The reaction mixture was heated on a water bath for 2 h, then poured into ice-cold water and acidified. The solid that separated was filtered off and crystallized.

2-(4-Amino-3-sulfanyl-4*H*-1,2,4-triazol-5-ylmethylthio)-4-chloro-8-methylquinoline (*XXIV*)

A mixture of *XIV* (0.01 mol), carbon disulfide (0.02 mol), and potassium hydroxide (5 cm^3, 10 %) in ethanol (30 cm^3) was refluxed on a water bath for only 1 h, afterwards hydrazine hydrate (0.015 mol) was added and the mixture was refluxed for another 3 h. The mixture was poured into ice-cold water and the solid so formed was filtered off and crystallized.

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