SYNTHESIS AND APPLICATION OF SOME NEW S-(SUBSTITUTED)-THIO- AND THIENOQUINOLINE DERIVATIVES AS ANTIMICROBIAL AGENTS

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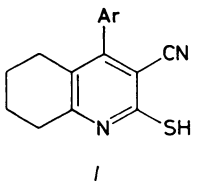
Received May 21, 1990
Accepted February 14, 1991

Ethyl (4-aryl-3-cyano-5,6,7,8-tetrahydro-2-quinolinylthio) acetate (*IIa, IIb*) were prepared and reacted with hydrazine hydrate to give hydrazides *IIIa, IIIb* which underwent cyclization into thienoquinoline derivatives *IVa, IVb*. Reaction of *IIIa, IIIb* with phenyl isocyanate yielded semicarbazides *Va, Vb*. Similarly, *IIIa, IIIb* and *IVb* were interacted with methyl/phenyl isothiocyanates affording the corresponding thiosemicarbazide derivatives *VIa—VId* and *XIVa, XIVb* respectively. On the other hand, condensation of *IIIb* with acetylacetone gave the pyrazole *VII* which upon treatment with ethoxide furnished *VIII*. Also, *IIIa, IIIb* and *IVa, IVb* reacted with aromatic aldehydes to afford hydrazones *IXa—IXf* and *XIa—XIf* respectively. Cyclodehydration of *IXd—IXf* with thioglycolic acid furnished 4-thiazolidinone derivatives *Xa—Xc*. Moreover, *IVb* was reacted with formic acid/acetic anhydride to give *XII* and *XIII*. Diazotization of *IVb* gave azide *XV* which underwent Curtius rearrangement into *XVI*. The structures of all newly synthesized compounds were confirmed by elemental analyses and spectral data. Also, the most of these compounds were tested in vitro for their antimicrobial activities against some Gram-positive and Gram-negative bacteria.

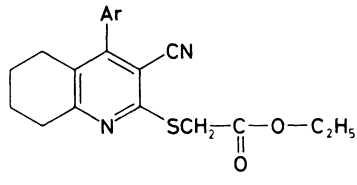
Some quinolines have been found to possess antimalarial, antifilarial and antihypertensive activities[1-4]. Also, many thiosemicarbazides are known for their good antibacterial[5,6], antifugal[7,8], herbicidal[9], antiacetylcholinesterase[10] and antitubercular[11] activities. Acid hydrazides and some arylidenes are reported to be exhibit antimicrobial activities[12-14]. Some thiazolidinone derivatives have been found to be biologically important compounds having anticonvulsant and tuberculostatic effects[15-18]. Morever, pyrazole derivatives have been associated with antifungal[19], antibacterial[20] and antimicrobial[21] activities. All these observations prompted us to synthesize the title compounds wherein biologically active moieties are present and to evaluate the antibacterial activities of them.

Reaction of 4-aryl-3-cyano-2-mercapto-5,6,7,8-tetrahydroquinolines (*Ia, Ib*) with ethyl chloroacetate in refluxing ethanol containing anhydrous sodium acetate gave the desired ethyl (4-aryl-3-cyano-5,6,7,8-tetrahydro-2-quinolinylthio)acetates (*IIa, IIb*). These esters (*IIa, IIb*) were reacted with hydrazine hydrate in absolute ethanol

to give (4-aryl-3-cyano-5,6,7,8-tetrahydro-2-quinolinylthio)acethydrazides (*IIIa*, *IIIb*). The precursors *IVa*, *IVb* were easily synthesized by cyclization of hydrazides *IIIa*, *IIIb* in refluxing ethanol containing anhydrous potassium carbonate.



I



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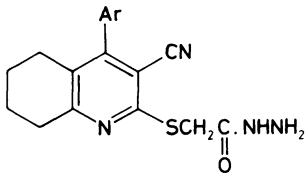
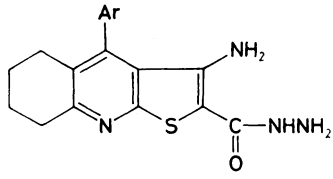


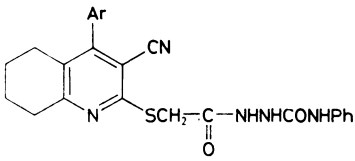
III



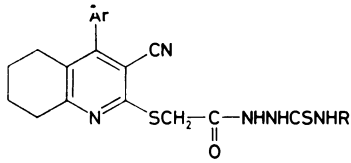
IV

In formulae *I*–*IV*: *a*, Ar = C_6H_5; *b*, Ar = 4-Cl—C_6H_4

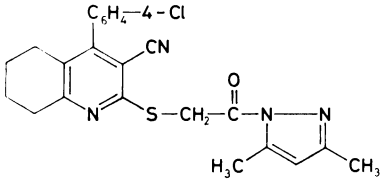
Reaction of hydrazides *IIIa*, *IIIb* with phenyl isocyanate yielded 1-(4-aryl-3-cyano-5,6,7,8-tetrahydro-2-quinolinylthio)acetyl-4-phenylsemicarbazides (*Va*, *Vb*). Similarely, *IIIa*, *IIIb* were reacted with methyl and/or phenyl isothiocyanate to give the corresponding thiosemicarbazides *VIa*–*VIf* in good yields. Condensation of *IIIb* with acetylacetone in refluxing ethanol gave 1-(3-cyano-4-*p*-chlorophenyl-5,6,7,8-tetrahydro-2-quinolinylthio)acetyl-3,5-dimethylpyrazole (*VII*) which upon cyclization with sodium ethoxide in ethanol furnished thienoquinoline *VIII*. The latter compound *VIII* was also synthesized by reaction of *IVb* with acetylacetone. Reaction of *IIIa*, *IIIb* with aromatic aldehydes by refluxing in ethanol yielded N^1-benzylidene-(4-aryl-3-cyano-5,6,7,8-tetrahydro-2-quinolinylthio)acethydrazides (*IXa*–*IXf*). Cyclodehydration of *IXd*–*IXf* with thioglycolic acid by refluxing in dry benzene for long time gave 4-thiazolidinone derivatives *Xa*–*Xc*. Compounds *IXa*–*IXf* on warming in ethanol containing sodium ethoxide, underwent smooth cyclization into N-benzylidene-3-amino-4-aryl-5,6,7,8-tetrahydro-thieno[2,3-*b*]quinoline-2-carbohydrazides (*XIa*–*XIf*). The latter compounds (*XIa*–*XIf*) were also confirmed by another synthetic route through reaction of *IVa*, *IVb* with aromatic aldehydes in refluxing ethanol.



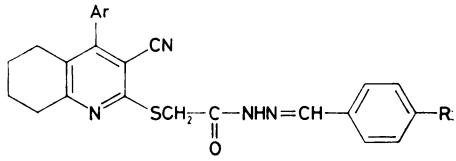
Va, Ar = C_6H_5
Vb, Ar = 4-Cl—C_6H_4



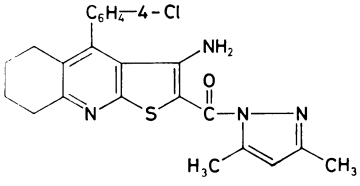
	Ar	R
VI a	C_6H_5	CH_3
VI b	C_6H_5	C_6H_5
VI c	4-Cl—C_6H_4	CH_3
VI d	4-Cl—C_6H_4	C_6H_5



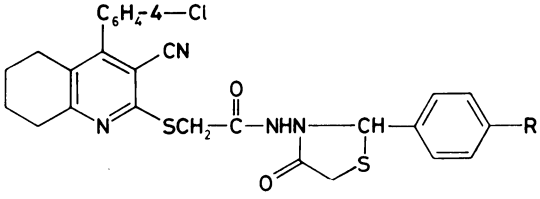
VII



	Ar	R
IX a	C_6H_5	H
IX b	C_6H_5	OCH_3
IX c	C_6H_5	Cl
IX d	4-Cl—C_6H_4	H
IX e	4-Cl—C_6H_4	OCH_3
IX f	4-Cl—C_6H_4	Cl



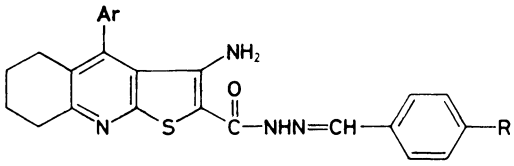
VIII



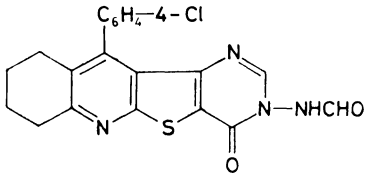
Xa, R = H
Xb, R = OCH_3
Xc, R = Cl

Furthermore, interaction of *IVb* with formic acid and/or acetic anhydride led to the formation of tetracyclic compounds *XII* and *XIII*, respectively. Also, *IVb* was

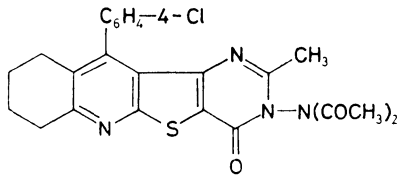
reacted with methyl and/or phenyl isothiocyanate giving 1-[(3-amino-4-*p*-chlorophenyl-5,6,7,8-tetrahydro-thieno[2,3-*b*]quinolin-2-yl)carbonyl]-4-substituted thiosemicarbazides (*XIVa*, *XIVb*) in nearly quantitative yields. Finally, treatment of *IV* in glacial acetic acid with sodium nitrite at room temperature gave 3-amino-4-*p*-chlorophenyl-5,6,7,8-tetrahydro-thieno[2,3-*b*]quinoline-2-carbonylazide (*XV*). Com-



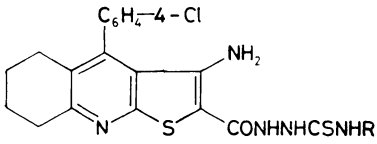
	Ar	R		Ar	R
XIa	C_6H_5	H	*XId*	4-Cl—C_6H_4	H
XIb	C_6H_5	OCH_3	*XIe*	4-Cl—C_6H_4	OCH_3
XIc	C_6H_5	Cl	*XIf*	4-Cl—C_6H_4	Cl



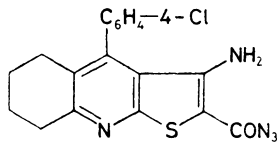
XII



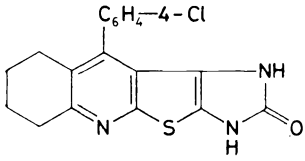
XIII



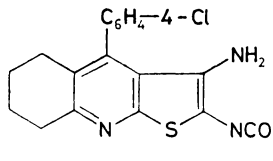
XIV a, R = CH_3
XIV b, R = C_6H_5



XV



XVI



XVII

pound *XV* underwent Curtius rearrangement in boiling tert-butyl alcohol into tetracyclic compound *XVI* through intermediate formation of isocyanate *XVII*.

The structures of all synthesized compounds were confirmed on the basis of their elemental analyses (Table I), IR and ^{1}H NMR spectra.

Biological Evaluation

Most of the synthesized compounds were evaluated for their antimicrobial activities against five strains of bacteria (Table II). The results indicated that most of the tested compounds exhibit mild to strong activities (inhibition zones ranged from 10 to 60 mm) against *Bacillus cereus, Micrococcus roseus* and *Staphylococcus aureus*. Some of the possess moderate to strong inhibitory effects (inhibition zones ranged from 20 to 70 mm) against *Escherichia coli*. Whereas all compounds being inactive against *Serratia rhodnii* except for *XV* which showed remarkable activity against it. Also, it is observed that all compounds containing thiophene ring (*VIII, XIa, XIf, XII, XIII, XIVa, XIVb* and *XV*) exhibited the strongest activities against *Bacillus cereus, Micrococcus roseus, Staphylococcus aureus, Escherichia coli* and no activity against *Serratia rhodnii*. Compounds *VIII, XIa, XIf, XIVa* and *XIVb* showed stronger potency than isomers *VII, IXa, IXf, VIc* and *VId*, respectively. Only compound *XV* showed considerable activities against all species.

EXPERIMENTAL

All melting points are uncorrected. The IR spectra were run on a Pye-Unicam SP 3-100 spectrophotometer using KBr disc technique (wavenumbers in cm^{-1}). The ^{1}H NMR spectra were recorded on a Varian EM-390 90 MHz ^{1}H NMR spectrometer using TMS as internal standard; chemical shifts are given in ppm (δ — scale). The physical constants and analytical data of all newly synthesized compounds are listed in Table I.

Ethyl (4-Aryl-3-cyano-5,6,7,8-tetrahydro-2-quinolinylthio)acetates (*IIa, IIb*)

A mixture of *Ia, Ib* (ref.[22], 10 mmol), ethyl chloroacetate (1·23 g, 10 mmol) and fused sodium acetate (3 g) in ethanol (100 ml) was refluxed for 2 h. On cooling, the crystalline solid thus formed was collected and recrystallized from ethanol as colourless needles of *IIa, IIb*. *IIa*: ^{1}H NMR spectrum ($CDCl_3$): 7·05—7·50 (m, 5 H, aromatic); 2·88 (t, 2 H, CH_2 at C-8); 2·38 (t, 2 H, CH_2 at C-5); 1·50—2·00 (m, 4 H, $(CH_2)_2$ at C-6, 7); 3·90 (s, 2 H, SCH_2); 4·17 (q, 2 H, $COOCH_2$) and 1·30 (t, 3 H, CH_3). The IR spectra of *IIa, IIb* showed the presence of two bands at 2 240 for (C≡N) and at 1 740 for (C=O).

(4-Aryl-3-cyano-5,6,7,8-tetrahydro-2-quinolinylthio)acethydrazides (*IIIa, IIIb*)

A mixture of *IIa, IIb* (10 mmol) and hydrazine hydrate 99% (0·5 ml, 10 mmol) in absolute ethanol (50 ml) was refluxed for 4 h. The reaction mixture was cooled in an ice bath and diluted with water (50 ml). The precipitate was filtered off and recrystallized from benzene as colourless plates. The IR spectra of *IIIa, IIIb* showed characteristic absorption bands at 3 260, 3 100 for ($NHNH_2$), at 2 240 for (C≡N) and at 1 660 for (C=O).

TABLE I

Physical constants and analytical data of the synthesized compounds

Compound	M.p. °C	Yield, % (Method *A*/ Method *B*)[b]	Formula (M.W.)	Calculated/Found				
				% C	% H	% N	% S	% Cl
IIa	109—110	90	$C_{20}H_{20}N_2O_2S$ (352·5)	68·16 68·50	5·72 5·37	7·95 7·90	9·10 9·00	— —
IIb	131[a]	96	$C_{20}H_{19}ClN_2O_2S$ (386·9)	62·09 62·41	4·95 4·90	7·24 7·53	8·29 8·35	9·16 9·31
IIIa	163—164	92	$C_{18}H_{18}N_4OS$ (338·4)	63·88 63·79	5·36 5·30	16·56 16·81	9·47 9·16	— —
IIIb	179—180	95	$C_{18}H_{17}ClN_4OS$ (372·9)	57·98 58·11	4·60 4·55	15·03 15·20	8·60 8·49	9·51 9·56
IVa	269—272	64	$C_{18}H_{18}N_4OS$ (338·4)	63·88 64·02	5·36 5·31	16·56 16·70	9·47 9·90	— —
IVb	298—300	60	$C_{18}H_{17}ClN_4OS$ (372·9)	57·98 57·78	4·60 4·66	15·03 14·87	8·60 8·91	9·51 9·83
Va	207—208	95	$C_{25}H_{23}N_5O_2S$ (457·5)	65·63 65·67	5·07 5·25	15·31 15·42	7·01 7·11	— —
Vb	235—236	97	$C_{25}H_{22}ClN_5O_2S$ (492·0)	61·03 61·20	4·51 4·60	14·23 14·49	6·52 6·62	7·21 7·30
VIa	222—224	95	$C_{20}H_{21}N_5OS_2$ (411·5)	58·37 58·28	5·14 5·17	17·02 17·20	15·58 15·66	— —
VIb	188—189	96	$C_{25}H_{23}N_5OS_2$ (473·6)	63·40 63·75	4·89 4·83	14·79 14·74	13·54 13·74	— —
VIc	228—230	93	$C_{20}H_{20}ClN_5OS_2$ (446·0)	53·86 53·80	4·52 4·44	15·70 15·75	14·38 14·31	7·95 8·01
VId	159—160	91	$C_{25}H_{22}ClN_5OS_2$ (508·1)	59·10 59·19	4·36 4·40	13·78 13·59	12·62 12·86	6·98 7·11
VII	183—185	78	$C_{23}H_{21}ClN_4OS$ (437·0)	63·22 63·03	4·84 4·82	12·82 12·55	7·34 7·37	8·11 8·00
VIII	290—291	90 93	$C_{23}H_{21}ClN_4OS$ (437·0)	63·22 63·33	4·84 4·80	12·82 12·66	7·34 7·46	8·11 8·20
IXa	138—140	85	$C_{25}H_{22}N_4OS$ (426·5)	70·40 70·31	5·20 5·17	13·14 13·42	7·52 7·60	— —
IXb	168—170	86	$C_{26}H_{24}N_4O_2S$ (456·6)	68·40 68·70	5·30 5·21	12·27 12·17	7·02 7·18	— —
IXc	227—228	83	$C_{25}H_{21}ClN_4OS$ (461·0)	65·14 65·46	4·59 4·63	12·15 12·25	6·95 7·14	7·69 7·91

TABLE I
(*Continued*)

Compound	M.p. °C	Yield, % (Method *A*/ Method *B*)[b]	Formula (M.W.)	Calculated/Found				
				% C	% H	% N	% S	% Cl
IXd	207—209	85	$C_{25}H_{21}ClN_4OS$	65·14	4·59	12·15	6·95	7·69
			(461·0)	65·28	4·59	12·00	7·25	7·81
IXe	180—182	91	$C_{26}H_{23}ClN_4O_2S$	63·60	4·72	11·41	6·53	7·22
			(491·0)	63·91	4·87	11·32	6·77	7·10
IXf	214—215	92	$C_{25}H_{20}Cl_2N_4OS$	60·61	4·07	11·31	6·47	14·31
			(495·4)	60·39	4·00	11·20	6·81	14·59
Xa	201	82	$C_{27}H_{23}ClN_4O_2S_2$	60·61	4·33	10·47	11·98	6·63
			(535·1)	60·50	4·51	10·40	11·87	6·87
Xb	240—243	79	$C_{28}H_{25}ClN_4O_3S_2$	59·51	4·46	9·91	11·35	6·27
			(565·1)	59·59	4·28	10·10	11·06	6·13
Xc	220	80	$C_{27}H_{22}Cl_2N_4O_2S_2$	56·94	3·89	9·84	11·26	12·45
			(569·5)	56·94	3·89	9·99	11·01	12·49
XIa	289—290	90	$C_{25}H_{22}N_4OS$	70·40	5·20	13·14	7·52	—
		81	(426·5)	70·09	5·15	13·27	7·30	—
XIb	261—262	92	$C_{26}H_{24}N_4O_2S$	68·40	5·30	12·27	7·02	—
		90	(456·6)	68·11	5·30	12·16	7·09	—
XIc	270—275	95	$C_{25}H_{21}ClN_4OS$	65·14	4·59	12·15	6·95	7·69
		85	(461·0)	65·34	4·42	12·43	7·21	7·39
XId	320	93	$C_{25}H_{21}ClN_4OS$	65·14	4·59	12·15	6·95	7·69
		89	(461·0)	65·17	4·61	12·51	7·15	7·60
XIe	293—295	94	$C_{26}H_{23}ClN_4O_2S$	63·60	4·72	11·41	6·53	7·22
		86	(491·0)	63·40	4·79	11·20	6·44	7·08
XIf	325	96	$C_{25}H_{20}Cl_2N_4OS$	60·61	4·07	11·31	6·47	14·31
		92	(495·4)	60·54	3·96	11·28	6·80	14·43
XII	185—186	83	$C_{20}H_{15}ClN_4O_2S$	58·47	3·68	13·64	7·80	8·63
			(410·9)	58·70	3·86	13·86	7·69	8·91
XIII	224—225	84	$C_{24}H_{21}ClN_4O_3S$	59·94	4·40	11·65	6·67	7·37
			(481·0)	60·09	4·41	11·50	6·46	7·11
XIVa	250—251	95	$C_{20}H_{20}ClN_5OS_2$	53·86	4·52	15·70	14·38	7·95
			(446·0)	54·04	4·50	15·59	14·06	8·19
XIVb	210	96	$C_{25}H_{22}ClN_5OS_2$	59·10	4·36	13·78	12·62	6·98
			(508·1)	59·36	4·26	13·80	12·79	7·29
XV	205 (dec.)	83	$C_{18}H_{14}ClN_5OS$	56·32	3·68	18·25	8·35	9·24
			(383·9)	59·39	3·71	18·02	8·51	9·07
XVI	>300	70	$C_{18}H_{14}ClN_3OS$	60·76	3·97	11·81	9·01	9·96
			(355·8)	61·02	4·00	11·71	9·30	9·82

[a] Literature[22] gives m.p. 132°C; [b] for compounds prepared by the two methods.

3-Amino-4-aryl-5,6,7,8-tetrahydro-thieno[2,3-*b*]quinoline-2-carbohydrazides (*IVa*, *IVb*)

To a solution of *IIIa*, *IIIb* (10 mmol) in absolute ethanol (100 ml), anhydrous potassium carbonate (3 g) was added. The mixture was refluxed for 2 h, filtered while hot. The filtrate was allowed to cool, the precipitated product was collected and recrystallized from ethanol as pale yellow needles. *IVb*: ^{1}H NMR spectrum ($CDCl_3$): 7·10—7·60 (m, 4 H, aromatic); 3·03 (t, 2 H, CH_2 at C-8); 2·37 (t, 2 H, CH_2 at C-5); 1·50—2·00 (m, 4 H, $(CH_2)_2$ at C-6, 7); 5·40 (s, 2 H, NH_2 at C-3 and exchangeable with D_2O); 3·90 (d, 2 H, NH_2 hydrazide, and exchangeable with D_2O). The IR spectra of *IVa*, *IVb* showed characteristic absorption bands at 3 500, 3 360 for (NH_2), at 3 240, 3 090 for ($NHNH_2$), at 1 620 for (C=O) and at 1 580 for (C=N).

TABLE II

Biological screening of the tested compounds (inhibition zones in mm). For further details see Experimental

Compound	*Bacillus cereus*	*Micrococcus roseus*	*Staphylococcus aureus*	*Escherichia coli*	*Serratia rhodnii*
IIa	20	15	20	—ve	—ve
IIb	20	10	—ve	—ve	—ve
IIIa	20	20	—ve	—ve	—ve
IIIb	60	20	—ve	—ve	—ve
IVb	30	20	—ve	30	—ve
Vb	—ve	—ve	10	20	—ve
VIa	30	—ve	20	—ve	—ve
VIb	—ve	15	10	—ve	—ve
VIc	20	—ve	20	—ve	—ve
VId	30	—ve	20	—ve	—ve
VII	—ve	30	10	30	—ve
VIII	10	30	20	70	—ve
IXa	20	10	20	—ve	—ve
IXf	20	20	20	—ve	—ve
Xa	20	10	—ve	20	—ve
Xc	—ve	—ve	—ve	20	—ve
XIa	20	20	20	—ve	—ve
XIf	20	10	10	20	—ve
XII	60	30	60	50	—ve
XIII	40	30	60	50	—ve
XIVa	20	60	40	50	—ve
XIVb	50	10	20	50	—ve
XV	30	20	40	20	20

—ve: Compound not effective.

1-(4-Aryl-3-cyano-5,6,7,8-tetrahydro-2-quinolinylthio)acetyl-4-phenylsemicarbazides (*Va*, *Vb*)

A mixture of *IIIa*, *IIIb* (5 mmol) and phenyl isocyanate (0·55 ml, 5 mmol) in absolute ethanol (30 ml) was refluxed for 3 h. White crystalline product obtained on cooling was recrystallized from ethanol. The IR spectra of *Va*, *Vb* showed characteristic absorption bands at 3 340, 3 285 for (NH groups), at 2 205 for (C≡N) and at 1 710, 1 670 (C=O groups).

1-(4-Aryl-3-cyano-5,6,7,8-tetrahydro-2-quinolinylthio)acetyl-4-
-substituted-3-thiosemicarbazides (*VIa*—*VId*)

A mixture of *IIIa*, *IIIb* (10 mmol) and methyl/phenyl isothiocyanate (10 mmol) in absolute ethanol (40 ml) was refluxed for 3 h. After cooling the solid thus formed wad colleced and recrystallized from ethanol in the form of white needles. The *VIa*: ^{1}H NMR spectrum (CF_3CO_2D): 7·15—7·60 (m, 5 H, aromatic); 2·60 (t, 2 H, CH_2 at C-5); 1·70—2·15 (m, 4 H, $(CH_2)_2$ at C-6, 7); 4·25 (s, 2 H, SCH_2) and 3·05—3·30 (m, 5 H, 2 H of CH_2 at C-8 and 3 H of $-CH_3$ group). The IR spectra of *VIa*—*VId* showed characteristic bands at 3 360, 3 200 for (NH groups), at 2 210 for (C≡N), at 1 720 for (C=O) and at 1 200 for (C=S).

1-(3-Cyano-4-*p*-chlorophenyl-5,6,7,8-tetrahydro-2-quinolinylthio)acetyl-
-3,5-dimethylpyrazole (*VII*)

A mixture of *IIIb* (3·73 g, 10 mmol) and acetylacetone (1 ml, 10 mmol) in ethanol (50 ml) was refluxed for 3 h. On concentration and cooling, the solid obtained was recrystallized from ethanol as pale yellow needles. IR spectrum: 2 210 for (C≡N) and 1 650 for (C=O).

1-[(3-Amino-4-*p*-chlorophenyl-5,6,7,8-tetrahydro-thieno[2,3-*d*]quinolin-
-2-yl)carbonyl]-3,5-dimethylpyrazole (*VIII*)

A) Compound *VII* (2·18 g, 5 mmol) in ethanol (50 ml) containing dissolved sodium (10 mg). The mixture was refluxed for 15 min. On cooling, the precipitate was collected and recrystallized from ethanol–chloroform mixture as yellow needles. ^{1}H NMR spectrum ($CDCl_3$): 7·10—7·50 (m, 4 H, aromatic); 3·07 (t, 2 H, CH_2 at C-8); 1·50—2·00 (m, 4 H, $(CH_2)_2$ at C-6, 7); 6·30 (s, 2 H, NH_2 and exchangeable with D_2O); 5·85 (s, 1 H, CH-pyrazole); 5·55 (s, 3 H, CH_3 attached to pyrazole ring); 2·35 (s, 5 H, 2 H of CH_2 at C-5 and 3 H of CH_3 group attached to pyrazole ring). IR spectrum: 3 500, 3 320 (NH_2); 1 630 (C=O); 1 590 (C=N).

B) A mixture of *IVb* (1·86 g, 5 mmol) and acetylacetone (1 ml, 10 mmol) was refluxed in ethanol for 4 h. The product obtained after cooling upon recrystallization was identical to that described in method *A*.

N^1-Benzylidene-(4-aryl-3-cyano-5,6,7,8-tetrahydro-2-quinolinylthio)-
acethydrazides (*IXa*—*IXf*)

To a solution of *IIIa*, *IIIb* (10 mmol) in ethanol (30 ml), an ethanolic solution of appropriate aldehyde (10 mmol) was added. The resulting mixture was refluxed for about 4 h. The solid formed on cooling was collected and recrystallized from ethanol as white needles. *IXe*: ^{1}H NMR spectrum ($CDCl_3$): 7·00—7·70 (m, 9 H, aromatic); 2·78 (t, 2 H, CH_2 at C-8); 2·38 (t, 2 H, CH_2 at C-5); 1·50—2·00 (m, 4 H, $(CH_2)_2$ at C-6, 7); 7·90 (s, 1 H, N=CH) and at 11·20 (s, 1 H, CONH and exchangeable with D_2O). The IR spectra of *IXa*—*IXf* showed characteristic absorption bands at 3 200 for (NH), at 2 220 for (C≡N), at 1 670 for (C=O) and at 1 600 for (C=).

2-Aryl-3-(3-cyano-4-*p*-chlorophenyl-5,6,7,8-tetrahydro-2-quinolinylthio)-acetamidothiazolidin-4-one (*Xa*—*Xc*)

A mixture of *IXd*—*IXf* (10 mmol) and thioglycolic acid (1·1 g, 12 mmol) in benzene (100 ml) was refluxed for 20 h, using Dean and Stark water-separator. The solvent was removed by distillation under reduced pressure. The residue was treated with sodium hydrogen carbonate solution, filtered off and crystallized from ethanol to give white needles of *Xa*—*Xc*. *Xc*: ^{1}H NMR spectrum ($CDCl_3$): 6·95—7·50 (m, 8 H, aromatic); 1·50—1·85 (m, 4 H, $(CH_2)_2$ at C-6, 7); 2·30—2·90 (m, 4 H: 2 H of CH_2 at C-8 and 2 H of CH_2 at C-5); 3·30—4·00 (m, 4 H: SCH_2 and CH_2 of thiazolidinone); 5·75 (s, 1 H, CH of thiazolidinone ring); 9·40 (s, 1 H, CONH and exchangeable with D_2O). The IR spectra of *Xa*—*Xc* showed chracteristic bands at 3 220 for (NH), 2 220 for (C≡N), at 1 730 for (C=O, thiazolidinone) and at 1 690 for (C=O, amide).

N^1-Benzylidene-3-amino-4-aryl-5,6,7,8-tetrahydro-thieno[2,3-*b*]quinoline--2-carbohydrazides (*XIa*—*XIf*)

A) Compound *IXa*—*IXf* (10 mmol) was suspended in ethanol (40 ml) containing dissolved sodium (10 mg). The contents were refluxed for 15 min. On cooling, the solid obtained was recrystallized from ethanol–chloroform mixture. The IR spectra of *XIa*—*XIf* showed characteristic absorption bands at 3 500, 3 340 for (NH_2), at 3 140 for (NH), at 1 620 for (C=O) and at 1 600, 1 580 for (C=N).

B) A mixture of *IVa*, *IVb* (10 mmol) and aromatic aldehyde (10 mmol) in ethanol (50 ml) was refluxed for 2 h. The precipitate formed on cooling was collected and recrystallized from ethanol–chloroform mixture. The products obtained by two synthetic routes are identical in all aspects.

3-Formylamino-11-*p*-chlorophenyl-7,8,9,10-tetrahydroquinolino-[3′,2′ : 4,5]thieno[3,2-*d*]pyrimidin-4(3*H*)-one (*XII*)

Compound *IVb* (1·86 g, 5 mmol) was refluxed for 4 h, with formic acid (20 ml). The reaction mixture was diluted with water, and the precipitate was recrystallized from benzene–light petroleum (40 : 60). ^{1}H NMR spectrum ($CDCl_3$): 7·25 (q, 4 H, aromatic); 3·10 (t, 2 H, CH_2 at C-7); 2·50 (t, 2 H, CH_2 at C-10); 1·60—2·00 (m, 4 H, $(CH_2)_2$ at C-8, 9); 7·70 (s, 1 H, CH or formyl group); 8·30 (s, 1 H, CH of pyrimidine). IR spectrum: 3 250 (NH); 1 720 (C=O, formyl group); 1 680 (C=O, pyrimidinone).

2-Methyl-3-diacetylamino-11-*p*-chlorophenyl-7,8,9,10-tetrahydroquinolino-[3′,2′ : 4,5]thieno[3,2-*d*]pyrimidin-4(3*H*)-one (*XIII*)

A suspension of *IVb* (1·86 g, 5 mmol) in redistilled acetic anhydride (20 ml) was refluxed for 3 h. The reaction mixture was cooled, diluted with water. The solid precipitate formed was collected and recrystallized from ethanol into colourless needles. ^{1}H NMR spectrum ($CDCl_3$): 7·27 (q, 4 H, aromatic); 3·15 (t, 2 H, CH_2 at C-7); 2·27 (t, 2 H, CH_2 at C-10); 1·50—1·90 (m, 4 H, $(CH_2)_2$ at C-8,9); 2·35 (s, 6 H, 2 × $COCH_3$); 2·00 (s, 3 H, CH_3). IR spectrum: 1 740 (C=O, acetyl groups); 1 690 (C=O, pyrimidinone).

1-[(3-Amino-4-*p*-chlorophenyl-5,6,7,8-tetrahydro-thieno[2,3-*b*]quinolin-2-yl)carbonyl]-4--substituted-3-thiosemicarbazides (*XIVa*, *XIVb*)

A mixture of *IVb* (1·86 g, 5 mmol) and methyl/phenyl isothiocyanate (5 mmol) in ethanol (30 ml)

was refluxed for 3 h. On cooling, the yellow precipitate formed was filtered off, dried and recrystallized from ethanol–chloroform into yellow needles. The IR spectra of *XIVa*, *XIVb* showed characteristic absorption bands at 3 200—3 100 (NH); 1 630 (C=O); 1 590 (C=N); 1 220 (C=S).

4-Amino-4-*p*-chlorophenyl-5,6,7,8-tetrahydro-thieno[2,3-*b*]quinolin-2-carbonylazide (*XV*)

Sodium nitrite solution (7 ml, 10%, 10 mmol) was added to a solution of *IVb* (3·7 g, 10 mmol) in acetic acid (10 ml) at room temperature during 5 min with stirring. The precipitated solid was filtered and crystallized from ethanol. IR spectrum: 3 500, 3 360 (NH_2); 2 110 (CON_3); 1 640 (C=O).

4-*p*-Chlorophenyl-5,6,7,8-tetrahydro-1*H*-imidazolo[4′,5′ : 4,5]thieno-[2,3-*b*]quinolin-2(3*H*)-one (*XVI*)

Compound *XV* (0·2 g, 0·5 mmol) was refluxed for 3 h in tert-butanol (20 ml). The reaction mixture was diluted with water (20 ml), the precipitate was collected and recrystallized from N,N-dimethylformamide–methanol mixture. ^{1}H NMR spectrum (CD_3SOCD_3): 7·30 (q, 4 H, aromatic); 2·90 (t, 2 H, CH_2 at C-8); 1·50—2·00 (m, 4 H, $(CH_2)_2$ at C-6, 7); 3·80 (s, 2 H, 2 × NH and exchangeable with D_2O). IR spectrum: 3 100—3 150 (NH); 1 670 (C=O).

Biological Screenining

Twenty-three compounds were screened in vitro for their antimicrobial activities against: *Bacillus cereus*, *Micrococcus roseus*, *Staphylococcus aureus*, *Escherichia coli* and *Serratia rhodnii* using paper disc diffusion method[23]. Sterilized 5 mm paper disc immersed in drug solution (20 mg in 1 ml of N,N-dimethylformamide) was placed in the petridish containing 25—30 ml of nutrient agar inoculated with 18—24 h test culture. Incubation was carried out at 37°C for 36 h and zones of inhibition was measured in mm.

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