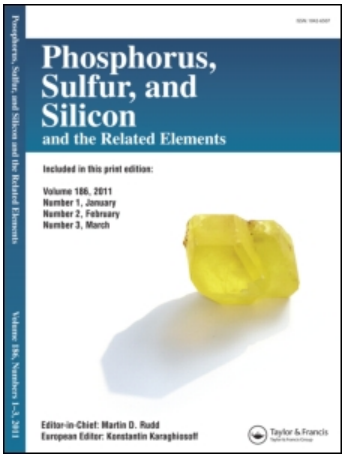

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BENZOQUINOLINES. I. SYNTHESIS AND REACTIONS OF SOME NEW FURYLBENZO[h]QUINOLINE DERIVATIVES

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BENZOQUINOLINES. I. SYNTHESIS AND REACTIONS OF SOME NEW FURYLBENZO[h]QUINOLINE DERIVATIVES

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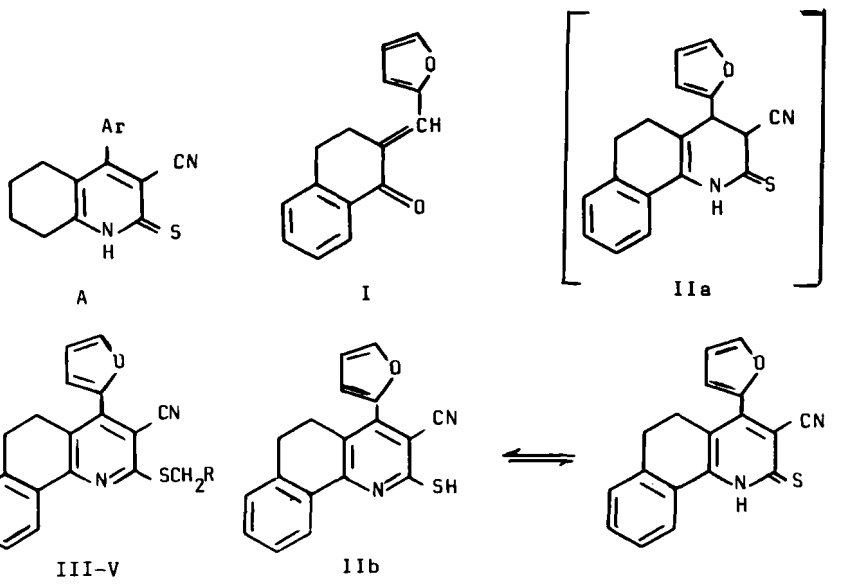
A series of new 3-cyano-5,6-dihydro-4-(2-furyl)-2-(substituted)thio-benzo[h]quinolines (**IIIa–IIIc**, **IV**, **V**, **VIIa–VIIe** and **IXa–IXc**) have been synthesized from 3-cyano-5,6-dihydro-4-(2-furyl)-benzo[h]quinoline-2(1H)-thione (**IIb**). Compounds **V**, **VIIa–VIIe** and **IXa–IXc** on treatment with appropriate base underwent smooth cyclization into thieno[2,3-b]-benzo[h]quinolines **VI**, **VIIIa–VIIIe** and **Xa–Xc**, respectively. Hydrolysis of ester **VI** gave the corresponding acid **XI** which was converted to oxazinone **XII** by heating in acetic anhydride. Oxazinone **XII**, in turn, was recyclized into pyrimidinone derivatives **XIII**, **XIV** and **XV** upon treatment with ammonium acetate, hydrazine hydrate and aniline, respectively. Compounds **Xa–Xc** were reacted with nitrous acid and with triethyl orthoformate to produce the fused polycyclic compounds **XVIa–XVIc** and **XVIIa–XVIIc**. The structures of all newly synthesized compounds were confirmed by elemental analyses and spectral data.

Key words: Furylbenzoquinolines; thienobenzoquinolines; pyrimidothienobenzoquinolines; triazinothienobenzoquinolines.

Recently, a number of reports concerning the synthesis of 4-aryl-3-cyano-5,6,7,8-tetrahydroquinoline-2(1H)-thiones(A) have appeared owing to their broad synthetic utility.[1–4] We report here the synthesis of their benzo-analogue **IIb** which was used as a versatile compound for synthesizing other benzo[h]quinolines of expected medicinal and biological importance.

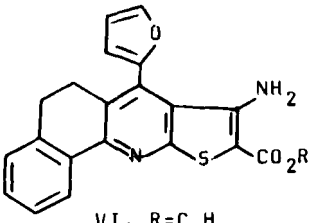


†Author to whom correspondence should be addressed.

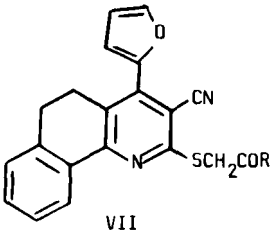
The starting compound, 3-cyano-5,6-dihydro-4-(2-furyl)-benzo[h]quinoline-2(1H)-thione (**IIb**) was synthesized by reaction of 2-furfurylidene-α-tetralone (**I**) with cyanothioacetamide in the presence of triethylamine as a basic catalyst. This reaction proceeds through the formation of tetrahydro derivative **IIa** which can't be isolated under the applied experimental conditions.

In formulas III-V:

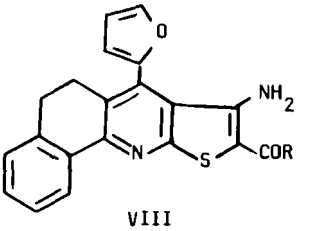
IIIa, R=H
IIIb, R=CH_3
IIIc, R=C_6H_5
IV , R=CH_2CN
V , R=$CO_2C_2H_5$



VI, R=C_2H_5
XI, R=H

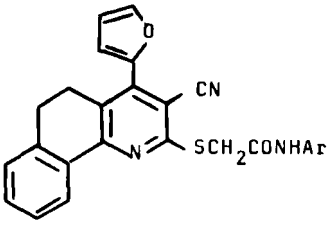


VII

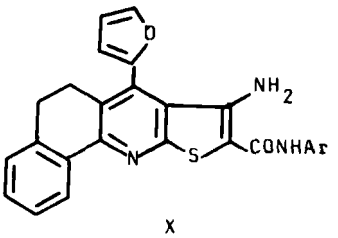


VIII

In formulae VII and VIII: a, R=CH_3;b, R=C_6H_5; c, R = 4-Cl-C_6H_4
d, R=4-Br-C_6H_4; e, R=8-hydroxy-4-quinolinyl.

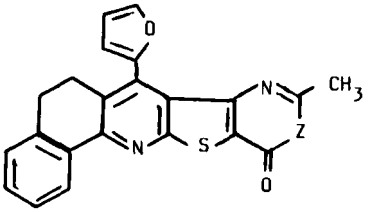


IX

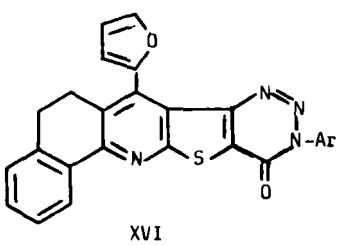


X

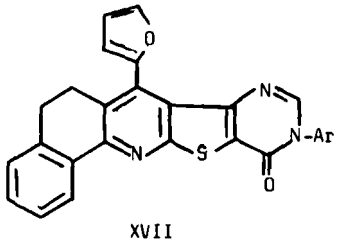
In formulae IX and X : a, Ar = C_6H_5; b, Ar = 4-CH_3-C_6H_4;
c, Ar = 4-Cl-C_6H_4.



XII, Z=O XIV, Z=N-NH_2
XIII, Z=NH XV, Z=N-C_6H_5



XVI



XVII

In formulae XVI and XVII : a, Ar = C_6H_5; b, 4-CH_3-C_6H_4; c, Ar = 4-Cl-C_6H_4

Reaction of compound **IIb** with some alkylating agents namely; methyl iodide, ethyl iodide and benzyl bromide in refluxing ethanol containing anhydrous sodium acetate gave the corresponding *S*-alkylated products **IIIa–IIIc** in excellent yields. 3-Cyano-2-cyanoethylthio-5,6-dihydro-4-(2-furyl)-benzo[h]quinoline (**IV**) was obtained by reaction of **IIb** with acrylonitrile under the same conditions. Compound **IIb** was reacted with ethyl chloroacetate to produce ester **V** which was then cyclized into the thieno[2,3-b]-benzo[h]quinoline derivative **VI** by treatment with sodium ethoxide in boiling ethanol.

Compound **IIb** was reacted with some α-haloketones namely; chloroacetone, *w*-bromoacetophenones and 4-chloroacetyl-8-hydroxyquinoline to yield *S*-substituted products **VIIa–VIIe** in good yields. The compounds **VIIa–VIIe** were readily cyclized into 2-acetyl(aroyl)-3-amino-5,6-dihydro-4-(2-furyl)-thieno[2,3-b]-benzo[h]-quinolines (**VIIIa–VIIIe**) by heating with potassium carbonate in ethanol. The latter compounds (**VIIIa–VIIIe**) were also obtained *via* direct reaction of **IIb** with the respective α-haloketone in refluxing ethanol containing potassium carbonate. The 2-arylcarbamoylmethylthio-3-cyano-5,6-dihydro-4-(2-furyl)-benzo[h]quinolines (**IXa–IXc**) were synthesized by the reaction of **IIb** with chloroacetanilide and its derivatives. Cyclization of compounds **IXa–IXc** into 3-amino-2-arylcarbamoyl-5,6-dihydro-4-(2-furyl)-thieno[2,3-b]-benzo[h]quinolines (**Xa–Xc**) was achieved in refluxing ethanol in the presence of sodium ethoxide.

Saponification of ethyl 3-amino-5,6-dihydro-4-(2-furyl)-thieno[2,3-b]-benzo[h]quinoline-2-carboxylate (**VI**) by heating in ethanolic sodium hydroxide solution yielded the sodium salt of the corresponding acid which gave the carboxylic acid **XI** on acidification. Heating of acid **XI** in acetic anhydride at reflux temperature led to the formation of 11,12-dihydro-13-(2-furyl)-2-methyl-4-oxy-oxazino[4′,5′:4,5]-thieno[2,3-b]-benzo[h]quinoline (**XII**). This oxazinone (**XII**) underwent ring transformation into pyrimidinones upon treatment with some amines. Interaction of **XII** with ammonium acetate in boiling acetic acid furnished pyrimidinone derivative **XIII**. Similarly, oxazinone **XII** on treatment with hydrazine hydrate underwent smooth recyclization to yield 3-amino-13-(2-furyl)-2-methyl-3,4,11,12-tetrahydro-4-oxopyrimido[4′,5′:4,5]-thieno[2,3-b]-benzo[h]quinoline (**XIV**). Oxazinone **XII** was converted into pyrimidinone **XV** by heating with aniline in acetic acid.

Diazotization of the precursors **Xa–Xc** with sodium nitrite-hydrochloric acid in acetic acid furnished 3-aryl-13-(2-furyl)-3,4,11,12-tetrahydro-4-oxo-1,2,3-triazino[4′,5′:4,5]-thieno[2,3-b]-benzo[h]quinolines (**XVIa–XVIc**). Compounds **Xa–Xc**

TABLE I

Characterization data of the prepared compounds

Compound	M.P. (°C) Yield (%)	Formula (M.W.)	Calculated/Found %C	%H	%N	%S	%Br(Cl)
IIb	228-9	$C_{18}H_{12}N_2OS$	71.03	3.97	9.20	10.53	—
	(73)	(304.4)	71.21	3.92	9.34	10.43	—
IIIa	188	$C_{19}H_{14}N_2OS$	71.67	4.43	8.80	10.07	—
	(82)	(318.4)	71.62	4.45	8.55	10.09	—
IIIb	170	$C_{20}H_{16}N_2OS$	72.26	4.85	8.43	9.64	—
	(85)	(332.4)	72.03	4.86	8.71	9.56	—
IIIc	157	$C_{25}H_{18}N_2OS$	76.12	4.59	7.10	8.12	—
	(84)	(394.4)	76.05	9.57	7.11	8.32	—
IV	185-6	$C_{21}H_{15}N_3OS$	70.57	4.23	11.76	8.97	—
	(90)	(357.4)	70.46	4.23	12.01	9.18	—
V	135-6	$C_{22}H_{18}N_2O_3S$	67.67	4.64	7.16	8.21	—
	(79)	(390.4)	67.71	4.60	7.15	8.06	—
VI	187-8	$C_{22}H_{18}N_2O_3S$	67.67	4.64	7.16	8.21	—
	(93)	(390.4)	67.44	4.55	7.32	8.00	—
VIIa	150	$C_{21}H_{16}N_2O_2S$	69.98	4.47	7.77	8.90	—
	(78)	(360.4)	70.23	4.32	7.58	9.15	—
VIIb	216	$C_{26}H_{18}N_2O_2S$	73.91	4.29	6.63	7.59	—
	(79)	(422.5)	73.90	4.28	6.75	7.86	—
VIIc	171	$C_{26}H_{17}ClN_2O_2S$	68.34	3.75	6.13	7.02	7.76
	(82)	(456.9)	68.68	3.83	6.25	6.89	7.58
VIId	188-9	$C_{26}H_{17}BrN_2O_2S$	62.28	3.42	5.59	6.39	15.93
	(90)	(501.4)	62.11	3.49	5.78	6.64	16.05
VIIe	181	$C_{29}H_{19}N_3O_3S$	71.15	3.91	8.58	6.55	—
	(87)	(489.5)	71.47	3.98	8.77	6.35	—
VIIIa	160	$C_{21}H_{16}N_2O_2S$	69.98	4.47	7.77	8.90	—
	(93)	(360.4)	69.98	4.27	7.71	8.79	—
VIIIb	205	$C_{26}H_{18}N_2O_2S$	73.91	4.29	6.63	7.59	—
	(93)	(422.5)	73.60	4.51	6.81	7.66	—
VIIIc	201	$C_{26}H_{17}ClN_2O_2S$	68.34	3.75	6.13	7.02	7.76
	(91)	(456.9)	68.06	3.76	6.52	7.15	7.83
VIIId	223	$C_{26}H_{17}BrN_2O_2S$	62.28	3.42	5.59	6.39	15.93
	(90)	(501.4)	62.06	3.57	5.85	6.30	15.76
VIIIe	280	$C_{29}H_{19}N_3O_3S$	71.15	3.91	8.58	6.55	—
	(88)	(489.5)	70.87	3.79	8.44	6.42	—
IXa	216	$C_{26}H_{19}N_3O_2S$	71.38	4.38	9.60	7.33	—
	(80)	(437.5)	71.53	4.58	9.49	7.51	—
IXb	215	$C_{27}H_{21}N_3O_2S$	71.82	4.69	9.31	7.10	—
	(87)	(451.5)	71.93	4.75	9.81	7.25	—
IXc	221	$C_{26}H_{18}ClN_3O_2S$	66.17	3.84	8.90	6.79	7.52
	(85)	(472.0)	66.05	3.85	8.77	7.05	7.50
Xa	245-6	$C_{26}H_{19}N_3O_2S$	71.38	4.38	9.60	7.33	—
	(93)	(437.5)	71.28	4.21	9.43	7.29	—
Xb	220	$C_{27}H_{21}N_3O_2S$	71.82	4.69	9.31	7.10	—
	(90)	(451.5)	71.93	4.78	9.30	7.28	—
Xc	210	$C_{26}H_{18}ClN_3O_2S$	66.17	3.84	8.90	6.79	7.52
	(88)	(472.0)	66.00	3.82	9.17	6.92	7.60
XI	190	$C_{20}H_{14}N_2O_3S$	66.30	3.89	7.72	8.85	—
	(78)	(362.4)	66.35	3.91	7.44	9.10	—
XII	210	$C_{22}H_{14}N_2O_3S$	68.38	3.65	7.24	8.30	—
	(78)	(386.4)	68.66	3.61	7.51	8.00	—
XIII	>300	$C_{22}H_{15}N_3O_2S$	68.55	3.92	10.90	8.31	—
	(83)	(385.4)	68.73	3.94	10.67	8.18	—
XIV	285	$C_{22}H_{16}N_4O_2S$	65.98	4.03	13.99	8.00	—
	(80)	(400.4)	66.09	4.13	13.87	8.21	—
XV	290	$C_{28}H_{19}N_3O_2S$	72.87	4.15	9.10	6.95	—
	(97)	(461.5)	72.98	4.19	9.29	7.15	—

TABLE I (*Continued*)

Compound	M.P. (°C) Yield (%)	Formula (M.W.)	Calculated/Found %C	%H	%N	%S	%Br(Cl)
XVIa	264	$C_{26}H_{16}N_4O_2S$	69.63	3.60	12.50	7.15	—
	(85)	(448.5)	69.81	3.65	12.50	7.39	—
XVIb	285	$C_{27}H_{18}N_4O_2S$	70.12	3.91	12.11	6.93	—
	(80)	(462.4)	70.32	4.05	12.20	7.15	—
XVIC	235(d)	$C_{26}H_{15}ClN_4O_2S$	64.66	3.13	11.60	6.64	7.34
	(81)	(482.9)	64.95	3.16	11.51	6.69	7.42
XVIIa	283	$C_{27}H_{17}N_3O_2S$	72.47	3.83	9.40	7.16	—
	(86)	(447.5)	72.46	3.81	9.32	7.46	—
XVIIb	245	$C_{28}H_{19}N_3O_2S$	72.88	4.14	9.10	6.94	—
	(80)	(461.4)	72.93	4.11	9.38	7.15	—
XVIIc	266	$C_{27}H_{16}ClN_3O_2S$	67.28	3.34	8.72	6.65	7.36
	(83)	(481.9)	67.31	3.41	8.92	6.49	7.50

TABLE II

IR and ^{1}H-NMR spectral data

Compound	Spectral data*
IIb	IR:3 180(NH); 2 220(C≡N). ^{1}H-NMR: 7.90, 7.10, 6.70 (three multiplets equivalent to three furan protons); 7.20–7.80 m, 4H(arom.), 2.90 m, 4H(CH_2—CH_2).
IIIa	IR:2 220(C≡N); 1 590(C=N)
IIIb	IR:2 220(C≡N); 1 590(C=N). ^{1}H-NMR: 8.33, 6.95, 6.60 (three multiplets equivalent to three protons of furan ring); 7.15–7.70 m, 4H(arom.); 3.23–3.55 q, 2H(SCH_2), 2.70–3.15 m, 4H(CH_2—CH_2); 1.40–1.60 t, 3H(CH_3).
IIIc	IR:2 220(C≡N); 1 580(C=N).
IV	IR:2 220(C≡N); 2 240(C≡N).
V	IR:2 220(C≡N); 1 740(C=O). ^{1}H-NMR: 8.33, 6.95, 6.60 (three multiplets equivalent to the protons of furan ring); 7.15–7.70 m, 4H(arom.); 4.05–4.33 q, 4H(2 × CH_2); 2.70–3.15 m, 4H(CH_2—CH_2), 1.15–1.40 t, 3H(CH_3)
VI	IR:3 490, 3 360(NH_2), 1 665(C=O). ^{1}H-NMR: 8.45 m, 1H(furan proton); 6.60 m, 2H (furan protons); 7.15–7.75 m, 4H(arom.); 5.75 s, 2H(NH_2); 4.02–4.45 q, 2H(CH_2); 2.85 t, 4H(CH_2—CH_2); 1.30–1.45 t, 3H(3H).
VIIa	IR:2 230(C≡N); 1 725(C=O).
VIIb	IR:2 210(C≡N); 1 690(C=O).
VIIc	IR:2 220(C≡N); 1 700(C=O).
VIId	IR:2 210(C≡N); 1 690(C=O).
VIIe	IR:2 220(C≡N); 1 650(C=O). ^{1}H-NMR: 6.60, 6.95, 8.45 (three multiplets equivalent to the protons of furan ring); 4.85 s, 2H(SCH_2); 7.10–7.80 m, 7H(aromatic); 8.75 m, 1H(CH-quinoline); 9.35 m, 1H(CH-quinoline); 3.50 s, 1H(OH); 2.70–3.10 m, 4H(CH_2—CH_2).
VIIIa	IR:3 420, 3 340(NH_2); 1 640(C—O).
VIIIb	IR:3 450, 3 240(NH_2); 1 610(C=O). ^{1}H-NMR: 7.20–8.00 m, 9H(arom.); 8.40 m, 1H(furan proton). 6.90 s, 2H(NH_2); 6.70 m, 2H(furan protons), 2.90 m, 4H(CH_2—CH_2).
VIIIc	IR:3 440, 3 240(NH_2); 1 600(C=O).
VIIId	IR:3 440, 3 240(NH_2); 1 610(C=O).
VIIIe	IR:3 450, 3 240(NH_2); 1 610(C=O).
IXa	IR:3 290(NH); 2 225(C≡N); 1 665(C=O).

TABLE II (*Continued*)

Compound	Spectral data*
IXb	IR:3 280(NH); 2 225(C≡N); 1 665(C=O).
IXc	IR:3 280(NH); 2 225(C≡N); 1 665(C=O).
Xa	IR:3 480, 3 340(NH_2); 1 645(C=O). ^{1}H-NMR = 7.00–7.80 m, 9H(arom.); 8.45 m, 1H(furan proton); 6.65 m, 2H(furan protons); 6.00 s, 2H(NH_2); 2.85 m, 4H(CH_2—CH_2).
Xb	IR:3 480, 3 350(NH_2); 1 645(C=O).
Xc	IR:3 480, 3 350(NH_2); 1 650(C=O).
XI	IR:3 480, 3 340(NH_2); 1 640(C=O).
XII	IR:1 740(C=O); 1 610(C=N).
XIII	IR:3 200, 2 400(NH, br); 1 650(C=O).
XIV	IR:3 320, 3 210(NH_2); 1 660(C=O).
XV	IR:1 670(C=O). ^{1}H-NMR: 8.50 m, 1H(furan proton); 7.15–7.70 m, 9H(arom.); 6.45 m, 2H(furan protons); 2.85–3.15 m, 4H(CH_2—CH_2); 2.10 s, 3H(CH_3).
XVIa	IR:1 675(C=O). ^{1}H-NMR; 8.50 m, 1H(furan proton); 7.15–7.70 m, 9H(arom.); 6.65 m, 2H(furan protons); 2.85–3.15 m, 4H(CH_2—CH_2).
XVIb	IR:1 670(C=O).
XVIc	IR:1 675(C=O).
XVIIa	IR:1 670(C=O). ^{1}H-NMR: 8.50 m, 1H(furan proton); 8.10 s, 1H(CH of pyrimidinone ring); 7.15–7.70 m, 9H(arom.); 6.65 m, 2H(furan protons); 2.85–3.15 m, 4H(CH_2—CH_2).
XVIIb	IR:1 670(C=O).
XVIIc	IR:1 670(C=O).

*All ^{1}H-NMR spectra of the compounds were recorded in $CDCl_3$ as a solvent.

were easily condensed with triethyl orthoformate in refluxing acetic anhydride to give the pyrimidinones **XVIIa–XVIIc** in high yields. Heating of compound **Xa** in acetic anhydride led to the formation of the expected pyrimidinone **XV**.

Structural formulas of all compounds prepared were established and confirmed on the basis of their elemental analyses and spectral data (Tables I–III).

IR spectra of all compounds and ^{1}H-NMR spectra of some representative ones were in agreement with their proposed structures. It was observed that in the ^{1}H-NMR spectra of compounds **IIb**, **IIIb**, **V** and **VIIe**, the furan protons appeared as three multiplets while they appeared as two multiplets in the spectra of compounds **VI**, **VIIIb**, **Xa**, **XV**, **XVIa** and **XVIIa**. This difference may be due to the presence of a cyano group in the former compounds.

Mass spectra of compounds **IIb**, **IIIb**, **V**, **VI**, **VIIb**, **VIIe**, **Xa**, **XII**, **XV** and **XVIIa** showed molecular ion peaks (M^+). All *S*-substituted derivatives (**IIIb**, **V**, **VIIb** and **VIIe**) showed a peak at m/z 317 corresponding to the fragment (B) in Scheme XVIII. Also, both compound **XV** and **XVIIa** exhibited identical peaks with difference of m/z 14. For chosen examples, the fragmentation patterns are possible (Schemes XVIII–XX, Table III).

TABLE III

Relative intensity of the must prominent peaks of some representative compounds

Compound	m/z	RI	Compound	m/z	RI
IIb	304(M)	100	**Xa**	437(M)	55
	275(M—CHO)	55		345(M—PhNH)	100
IIIb	332(M)	39	**XII**	387(M)	100
	331(M—H)	100		386(M—H)	39
	317(M—H—CH_2)	21		343(M—CO_2)	16
	303(M—CHO)	10	**XV**	461(M)	100
	299(M—H—S)	23		488(M—CH)	19
	271(M—H—S—CO)	9		433(M—CO)	17
	242	12		417	11
V	390(M)	41		391	11
	317(M—$CO_2C_2H_5$)	100		344	15
VI	390(M)	90		315	15
	343	40		118	76
VIIb	422(M)	39		97	29
	387(M—COPh)	37		77($C_6H_5^+$)	66
	257	30		67	22
	150	40	**XVIIa**	447(M)	100
	129	42		419(M—CO)	24
	84	71		405(M—CO—N)	17
	69	100		315	20
VIIe	489(M)	68		104	18
	488(M—H)	100		85	8
	317(M—172)*	13		77($C_6H_5^+$)	49
	172	41		67	7

*172 = 8-hydroxy-4-quinolinyl carbonyl fragment.

EXPERIMENTAL

All melting points are uncorrected. The IR spectra were recorded in KBr on a Pye-Unicam SP3-100 spectrophotometer (wave number in cm^{-1}), ^{1}H-NMR spectra on a Varian EM-390 90 MHz spectrometer using TMS as internal standard (chemical shifts in δ, ppm) and mass spectra on Jeol JMS D-3000 spectrometer.

2-Furfurylidine-α-tetralone (**I**). This compound was prepared according to the literature method.[5]

3-Cyano-5,6-dihydro-4-(2-furyl)-benzo[h]quinoline-2(1H)-thione (**IIb**). To a mixture of chalcone **I** (4.50, 20 mmol) and cyanothioacetamide (2.0 g, 20 mmol) in abs. ethanol (70 ml), 2 ml of triethyl amine was added. The reaction mixture was refluxed for 6 h and allowed to stand overnight at room temperature. The solid obtained after subsequent concentration and cooling was filtered, washed with ethanol, dried and recrystallized from acetic acid in the form of red needles of **IIb**.

Reaction of compound **IIb** *with different halocompounds; formation of compounds* **IIIa–IIIc**, **V**, **VIIa–VIIc** *and* **IXa–IXc**:

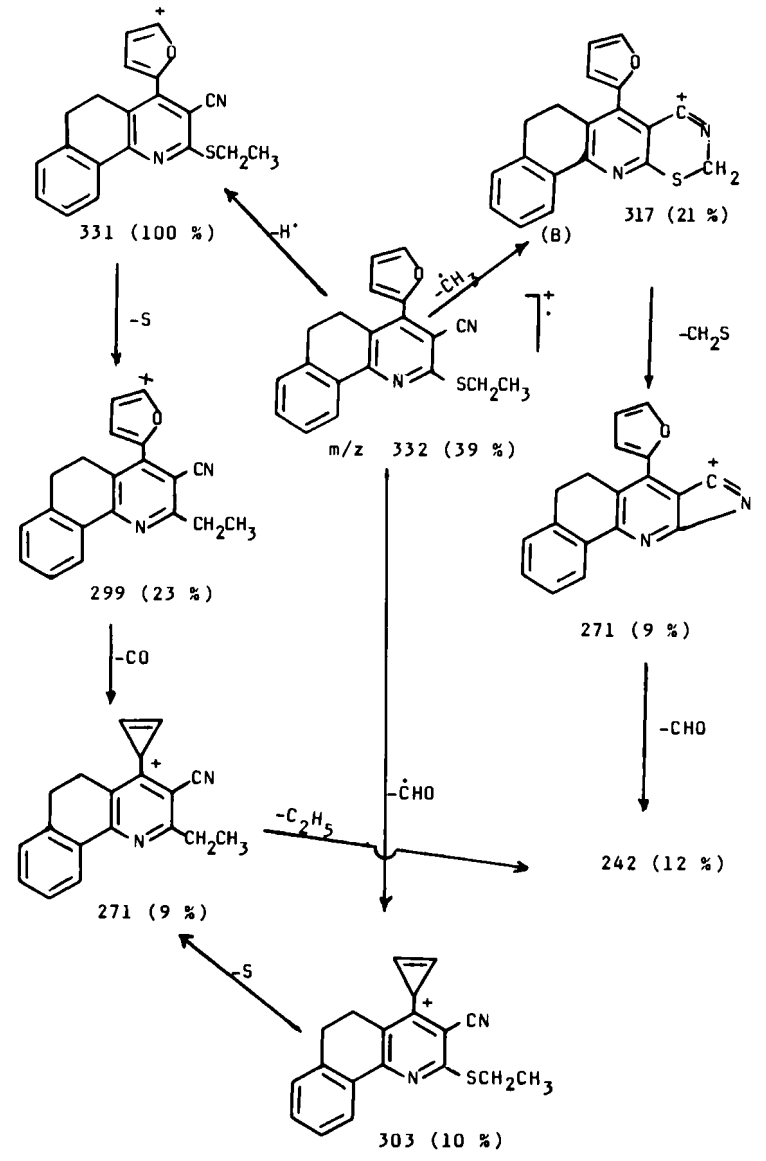
General procedure. A mixture of **IIb** (3.04 g, 10 mmol), respective halocompound (10 mmol) and anhydrous sodium acetate (1.25 g, 15 mmol) in ethanol (50 ml) was refluxed for 2 h; during reaction time the red color disappeared. On cooling, the precipitated product was collected by filtration, washed with water, air dried and recrystallized from ethanol as colorless needles. In this way the following compounds were synthesized:

a) 2-Alkyl/aralkyl thio-3-cyano-5,6-dihydro-4-(2-furyl)-benzo[h]quinolines (**IIIa–IIIc**) were synthesized by reaction of **IIb** with methyl iodide, ethyl iodide or benzyl bromide.

b) 2-Ethoxycarbonylmethylthio-3-cyano-5,6-dihydro-4-(2-furyl)-benzo[h]quinoline (**V**) obtained from the reaction of **IIb** with ethyl chloroacetate.

c) 2-Acetonylthio-3-cyano-5,6-dihydro-4-(2-furyl)-benzo[h]quinoline **VIIa** was obtained by the reaction of **IIb** with chloroacetone.

Compound IIIb:



Scheme XVIII

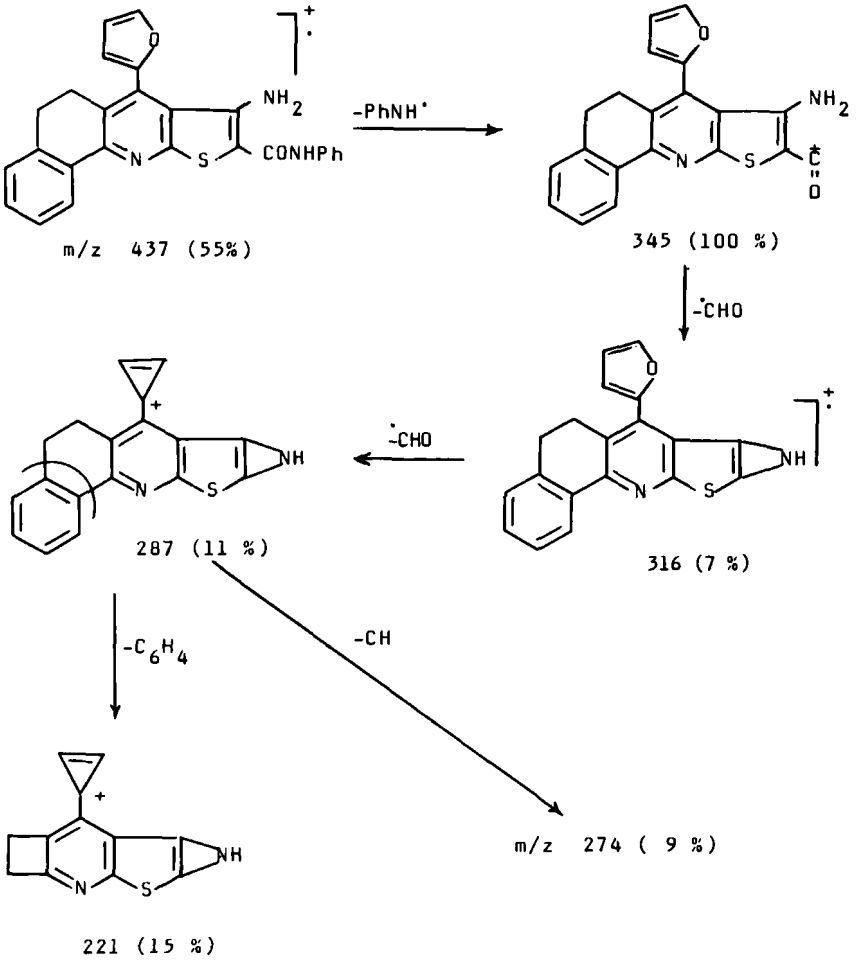
d) 2-Aroylmethylthio-3-cyano-5,6-dihydro-4-(2-furyl)-benzo[h]quinolines (**VIIb–VIId**) were synthesized by the reaction of **IIb** with phenacyl bromide, and the 4-chloro and 4-bromo derivatives.

e) 3-Cyano-5,6-dihydro-4-(2-furyl)-2-(8-hydroxy-4-quinolinyl)-acetylthio-benzo[h]quinoline (**VIIe**) was synthesized by the reaction of **IIb** with 4-chloroacetyl-8-hydroxyquinoline.

f) 2-Arylcarbamoylmethylthio-3-cyano-5,6-dihydro-4-(2-furyl)-benzo[h]quinolines (**IXa–IXc**) were synthesized by the reaction of **IIb** with chloroacetanilide, and the 4-methyl and 4-chloro derivatives.

3-Cyano-2-cyanoethylthio-5,6-dihydro-4-(2-furyl)-benzo[h]quinoline (**IV**). To a suspension of **IIb** (3.04 g, 10 mmol) and anhydrous sodium acetate (1.25, 15 mmol) in ethanol (60 ml), (10 mmol) of acrylonitrile

Compound Xa:



Scheme XIX

was added. The reaction mixture was refluxed for 3 h, then allowed to cool. The crystalline solid thus precipitated was collected by filtration, washed with water, dried in air and recrystallized from ethanol as colorless plates of **IV**.

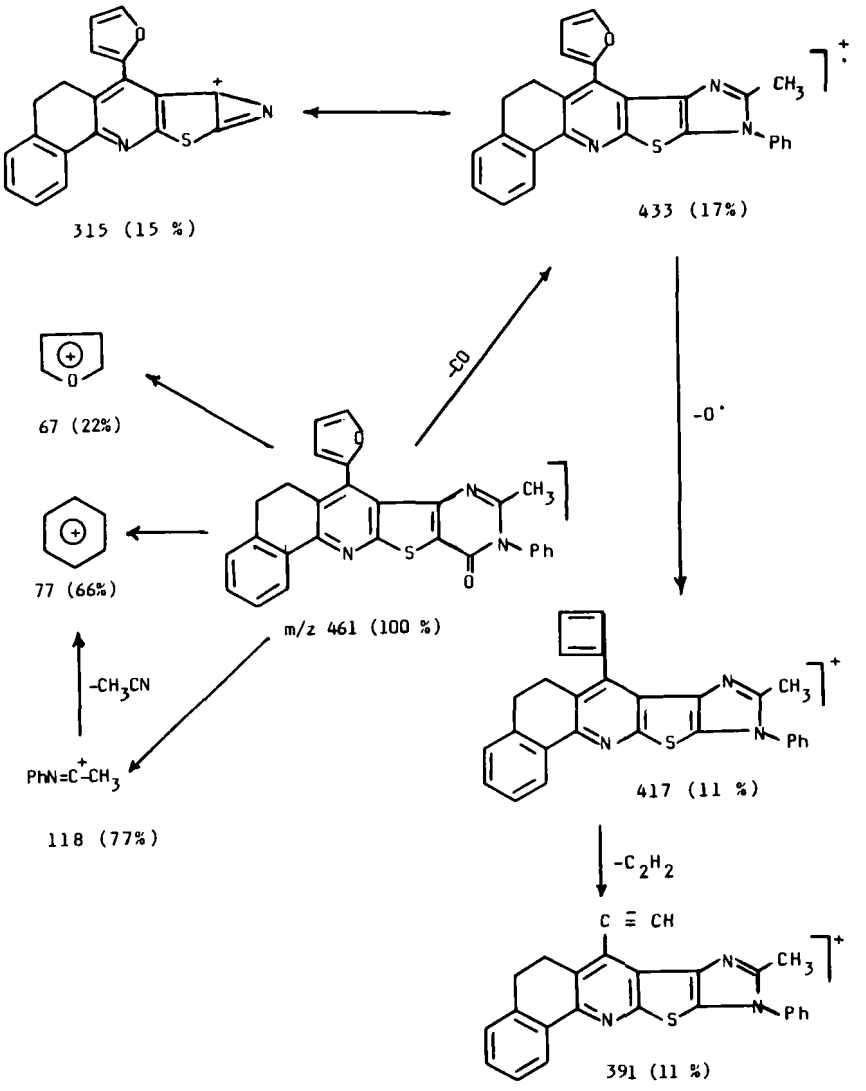
Ethyl 3-amino-5,6-dihydro-4-(2-furyl)-thieno[2,3-b]-benzo[h]quinoline-2-carboxylate (**VI**). Compound **V** (3.90 g, 10 mmol) in ethanol (50 ml) containing dissolved sodium (20 mg) was refluxed for 15 min. and then allowed to cool. The precipitate was collected and recrystallized from ethanol in the form of yellow needles of **VI**.

3-Amino-2-acetyl/aroyl-5,6-dihydro-4-(2-furyl)-thieno[2,3-b]-benzo[h]quinolines (**VIIIa–VIIId**):

A) A suspension of compounds **VIIa–VIId** (5 mmol) and anhydrous potassium carbonate (0.69 g, 5 mmol) in ethanol (40 ml) was refluxed for 30 min. The solids obtained after cooling were filtered off, washed with water and recrystallized from ethanol in the form of yellow needles of **VIIIa–VIIId**.

B) A mixture of **IIb** (1.52 g, 5 mmol), α-haloketone (5 mmol) and anhydrous potassium carbonate (1.38 g, 10 mmol) in ethanol (40 ml) was refluxed for 1 h. The solids separated upon recrystallization were identical to those described in method A).

Compound XV:



Scheme XX

3-Amino-5,6-dihydro-4-(2-furyl)-2-(8-hydroxy-4-quinolinyl)carbonylthieno[2,3-b]-benzo[h]quinoline **(VIIIe)**

A) Compound **VIIe** (2.45 g, 5 mmol) and anhydrous potassium carbonate (1.38 g, 10 mmol) in ethanol (50 ml) was refluxed for 1 h. The reaction mixture was cooled and acidified with dilute acetic acid and a solid product was precipitated. It was filtered off, washed with water, dried in air and recrystallized from chloroform-ethanol mixture as yellow prisms.

B) A mixture of **IIb** (1.52 g, 5 mmol), 4-chloroacetyl-8-hydroxyquinoline (1.11 g, 5 mmol) and anhydrous potassium carbonate (2.07, 15 mmol) in ethanol (50 ml) was refluxed for 2 h. The reaction mixture was cooled and acidified to form a solid product identical to that described in method A).

3-Amino-2-arylcarbamoyl-5,6-dihydro-4-(2-furyl)-thieno[2,3-b]-benzo[h]quinolines (**Xa–Xc**). A suspension of compounds **Xa–Xc** (7 mmol) in ethanol (50 ml) containing dissolved sodium (50 mg) was refluxed for 30 min. The precipitates obtained after cooling were collected and recrystallized from chloroform-ethanol in the form of yellow needles of **Xa–Xc**.

3-Amino-5,6-dihydro-4-(2-furyl)-thieno[2,3-b]-benzo[h]quinoline-2-carboxylic acid (**XI**). Compound **VI** (7.80 g, 20 mmol) in ethanolic sodium hydroxide (100 ml, 10%) was refluxed for 2 h. The reaction mixture was cooled and acidified and a solid product was precipitated. It was filtered, washed with water, dried in air and recrystallized from ethanol.

11,12-Dihydro-13-(2-furyl)-2-methyl-4-oxo-oxazino[4',5':4,5]-thieno[2,3-b]-benzo[h]quinoline (**XII**). Compound **XI** (5.43 g, 15 mmol) was refluxed for 4 h with acetic anhydride (100 ml). The reaction mixture was concentrated by distillation and allowed to cool. The crystalline solid obtained was applied in the next steps without further purification. A sample was recrystallized from absolute ethanol as colorless needles of **XII**.

13-(2-Furyl)-2-methyl-3,4,11,12-tetrahydro-4-oxopyrimido[4',5':4,5]-thieno[2,3-b]-benzo[h]quinoline (**XIII**). A mixture of **XII** (1.93 g, 5 mmol) and ammonium acetate (0.77 g, 10 mmol) in glacial acetic acid (20 ml) was refluxed for 3 h. On cooling, the white precipitate was collected by filtration, washed with water and recrystallized from ethanol as colorless needles of **XIII**.

3-Amino-13-(2-furyl)-2-methyl-3,4,11,12-tetrahydro-4-oxopyrimido[4',5':4,5]-thieno[2,3-b]-benzo[h]quinoline (**XIV**). A mixture of **XII** (1.93 g, 5 mmol) and hydrazine hydrate 99% (0.5 ml, 10 mmol) was refluxed in ethanol (20 ml) for 2 h. The product was recrystallized from ethanol in the form of colorless needles of **XIV**.

13-(2-Furyl)-2-methyl-3-phenyl-3,4,11,12-tetrahydro-4-oxopyrimido[4',5':4,5]-thieno[2,3-b]-benzo[h]quinoline (**XV**):

A) A mixture of **XII** (1.15 g, 3 mmol) and aniline (0.4 ml, 4 mmol) in glacial acetic acid (20 ml) was refluxed for 4 h. On cooling and dilution with water a white solid precipitated. It was filtered off and recrystallized from ethanol as white crystals of **XV**.

B) Compound **Xa** (0.88 g, 2 mmol) in redistilled acetic anhydride (20 ml) was refluxed for 3 h. The solid obtained upon recrystallization was identical in all aspects to that described in method A).

3-Aryl-13-(2-furyl)-3,4,11,12-tetrahydro-4-oxo-1,2,3-triazino[4',5':4,5]-thieno[2,3-b]-benzo[h]quinolines (**XVIa–XVIc**). To a solution of **Xa–Xc** (7 mmol) in concentrated hydrochloric acid (5 ml) and glacial acetic acid (5 ml) was added 10% sodium nitrite solution (7 ml, 10 mmol) at 0°C during 5 min with stirring. The white products obtained were crystallized from ethanol as white crystals of **XVIa–XVIc**.

3-Aryl-13-(2-furyl)-3,4,11,12-tetrahydro-4-oxopyrimido[4',5':4,5]-thieno[2,3-b]-benzo[h]quinolines (**XVIIa–XVIIc**). A mixture of **Xa–Xc** (5 mmol) and triethyl orthoformate (1 ml, 6 mmol) in acetic anhydride (25 ml) was refluxed for 3 h. The solids precipitated on cooling were collected and recrystallized from chloroform as white prisms of **XVIIa–XVIIc**.

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