Synthesis of Novel 2-Substituted Quinoline Derivatives: Antimicrobial, Inotropic, and Chronotropic Activities

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Three novel series of quinoline derivatives have been prepared by cyclization of the intermediate 3-(1,3-dioxolan-2-yl)-2-substituted thiocarbamoylhydrazinoquinolines with different α-halocarbonyl compounds. These series are: 3-(1,3-dioxolan-2-yl)-2-(3-substituted-4-phenylthiazolin-2-ylidene)hydrazinoquinolines; 3-(1,3-dioxolan-2-yl)-2-(3-substituted-5-ethoxycarbonyl-4-methylthiazoline-2-ylidene)hydrazinoquinolines and 3-(1,3-dioxolan-2-yl)-2-(3-substituted-4-thiazolidinon-2-yl)hydrazinoquinolines. The active methylene group of the latter series was used for the preparation of their arylidene derivatives. The antimicrobial as well as inotropic and chronotropic activities of the prepared compounds were studied.

Synthese von neuen 2-substituierten Chinolin-Derivaten: Antimikrobielle, inotropische und chronotropische Aktivität

Drei neue Serien von Chinolin-Derivaten wurden hergestellt durch Cyclisierung von 3-(1,3-Dioxolan-2-yl)-2-substituierten Thiocarbamoyl-hydrazinochinolinen mit verschiedenen α-Halocarbonyl-Verbindungen. Es handelt sich um 3-(1,3-Dioxolan-2-yl)-2-(3-substituierte-4-phenylthiazolin-2-yliden)hydrazinochinoline; 3-(1,3-Dioxolan-2-yl)-2-(3-substituierte-5-ethoxycarbonyl-4-methyl-2-yliden)-hydrazinochinoline und 3-(1,3-Dioxolan-2-yl)-2-(3-substituierte-4-thiazolidinon-2-yl) hydrazinochinoline. Ausgehend von der aktiven Methylengruppe der letztgenannten Serie, wurden die Aryliden-Derivate hergestellt. Die antimikrobielle, inotropische und chronotropische Aktivität der synthetisierten Verbindungen wurden studiert.

Considerable interest has been focused on quinoline derivatives which have been shown to possess a broad spectrum of biological activities. The most important are analgesic[1], antiinflammatory[2], antituberculous[3], antiprotozoal[4], antimalarial[5], and antibacterial[6] activities. Moreover, inotropic as well as chronotropic activtities have been recently attributed to some quinoline derivatives[7,8]. On the other hand, thiazole derivatives possess antithyroid[9], antimicrobial[10], and antifungal[11] activities, while thiazolidinone derivatives possess antibacterial[12], antihoemolytic[13], and hypnotic[14] effects.

Based on the abovementioned facts, we synthesized series of compounds containing the thiazoline or thiazolidinone moiety and a quinoline nucleus in one frame in order to study their antimicrobial, inotropic, and chronotropic activities.

For the synthesis of the target heterocycles, the reaction sequences outlined in scheme 1 were followed. Treatment of 2-chloroquinoline-3-carbaldehyde **1** with hydrazinehydrate never leads to the formation of the corresponding 2-hydrazino derivative and instead 1H-pyrazolo[3,4-b]quinoline [15] **2** was formed. So, in order to substitute the chlorine atom in compound **1** by a hydrazino group, protection of aldehydic groups was necessary. This was achieved by treating compound **1** with ethylene glycol/H^+ followed by reaction with hydrazine hydrate to afford 3-(1,3-dioxolan-2-yl)-2-hydrazinoquinoline (**4**). Treatment of **4** with substituted isothiocyanates afforded the corresponding 3-(1,3-dioxolan-2-yl)-2-substituted thiocarbamoylhydrazinoquinolines **5a-d**. **5a-d** are considered the key intermediates for the preparation of thiazoline and thiazolidinone derivatives by cyclization with α-halocarbonyl compounds. Thus, when **5a-d** were cyclized by phenacyl bromide, the 3-(1,3-dioxolan-2-yl)-2-(3-substituted-4-phenylthiazolin-2-ylidene)hydrazinoquinolines **6a-d** were formed. When ethyl α-chloroacetoacetate was used as a cyclizing agent, 3-(1,3-dixolan-2-yl)-2-(3-substituted-5-ethoxycarbonyl-4-methyl - thiazolin-2-ylidene)hydrazinoquinolines **7a, c, d** were obtained. On the other hand, when **5a-d** were cyclized with ethyl bromoacetate,3-(1,3-dioxolan-2-yl)-2-(3-substituted-4-thiazolidinon-2-ylidene)hydrazinoquinolines **8a-d** were obtained. The methylene group at the C-5-position of the 4-thiazolidinone moiety is known to be reactive toward aldol condensation[16]. Thus condensation of **8a-d** with aromatic aldehydes in the presence of a basic catalyst afforded the 3-(1,3-dioxolan-2-yl)-2-(3-substituted-5-arylidene-4-thiazolidinon-2-ylidene)hydrazinoquinolines **9a-i**. Acid cleavage of the dioxolane ring [17] of **9d, f, g, i** resulted in the formation of the corresponding 2-(3-substituted-5-arylidene-4-thiazolidinon-2-ylidene)hydrazinoquinoline-3-carbaldehydes **11a-d**. Compounds **11a-d** could be also be prepared from **8a-d** by first acid cleavage of the dioxolane ring followed by condensation with the proper aromatic aldehyde.

IR, ^{1}H-NMR and mass spectra of the prepared compounds are in agreement with the proposed structures (Experimental Part).

Biological evaluation

A Antimicrobial screening

The prepared compounds were evaluated for their antimicrobial activity by the agar diffusion method[18]. A 0.2%

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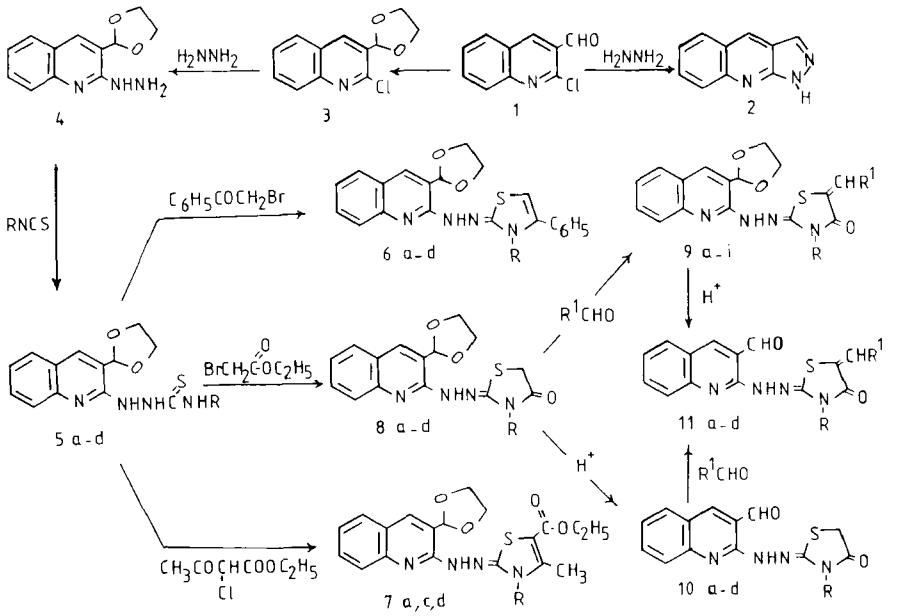

solution in propylene glycol was used. The test organisms were *Staphylococcus aureus* NCTC 4163, *Escherichia coli* NCTC 5933, and *Candida albicans* 3501. The resulting inhibition zones against *Staphylococcus aureus, Escherichia coli*, and *Candida albicans* were 15-22 mm; 15-19 mm; 14-20 mm respectively. Only compound **5d** showed high activity against *Staphylococcus aureus* (26 mm); while **5a** showed high activity against *Candida albicans* (25 mm). Compounds **7d** and **11b** were inactive against *Staphylococcus aureus*, while **5c, 6d, 7d** and **9h** were inactive against *Escherichia coli*. Compounds **5c, 5d, 6a-c, 7a, 7d, 8a-d, 9c, 9d, 9h, 10d, 11a** and **11c** were inactive against *Candida albicans*.

B Inotropic and chronotropic evaluation.

The compounds were preliminary tested for inotropic and chronotropic effects on the isolated frog heart[19] which was suspended in a 15 ml bath containing *Ringer* solution of 37°C, bubbled with carbogen. The compounds were dissolved in propylene glycol (2 mg/ml), then diluted with 3 ml of *Ringer* solution. The doses used were 5, 10, 20, 50, and 100 µg, respectively. Propylene glycol at this concentrations has no effect on the heart. - **5c** demonstrated a mild negative inotropic effect and **6c** exhibited a pronounced positive inotropic effect, while **8b** showed a pronounced negative chronotropic activity. However, the remaining compounds demonstrated no significant effect on the *Toad's* heart at the dose levels used.

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Experimental Part

Melting points are uncorrected. - IR spectra (Nujol): Beckman 4210. - ^{1}H-NMR: EM-360L and Bruker 200 MHz spectrometers in $CDCl_3$, TMS as intern. standard, chemical shift in δ(ppm). - Mass spectra: Mat-711 spectrometer, inlet temp. ca 200°C, ionization energy 70 e.v.-Analytical data: analytical Unit, Faculty of Science, Cairo University.

2-Chloro-3-(1,3-dioxolan-2-yl)quinoline (**3**)

A solution containing 2-chloroquinoline-3-carbaldehyde **1** (3.8 g, 0.02 mole), ethylene glycol (3.7 g, 0.06 mole), and a crystal of toluene p-sulphonic acid in benzene (100 ml) was heated under reflux for 5 h using a *Dean-Stark* separator. The mixture was cooled, washed with a saturated solution of Na_2CO_3 (50 ml) followed by water (100 ml) and then dried (Na_2SO_4). The solvent was removed by evaporation in vacuo and the residue was crystallized from aqueous ethanol (1:3), m.p. 59-60°C, yield (3.3 g, 70%). - IR: 1655; 1610; 1590 (C=N, C=C); 1215; 1180; 1135; 1035 (C-O-C). - ^{1}H-NMR: 4.0-4.3 (m, 4H, O-CH_2-CH_2-O), 6.2 (s, 1H, CH), 7.4-8.2 (m, 4H, Ar-H), 8.4 (s, 1H, H-4). - $C_{12}H_{10}ClNO_2$ (235.7) Calc. C 61.2 H 4.28 N 5.9 Cl 15.0 Found C 61.3 H 4.1 N 6.2 Cl 14.8.

3-(1,3-Dioxolan-2-yl)-2-hydrazinoquinoline (**4**)

A mixture of **3** (2.35 g, 0.01 mole) and hydrazine hydrate (4.9 ml, 0.1 mole) was heated under reflux for 20 min. The mixture was cooled to 0°C, diluted with ice-cold water (100 ml) and shaken vigorously for 5 min to solidify the oily residue. The separated product was filtered, washed thoroughly with water and crystallized from water, m.p. 69-70°C, yield (1.84 g, 80%). - IR: 3400-3150 (NH); 1610; 1575; 1510 (C=N; δNH, C=C); 1255; 1170; 1110; 1055 (C-O-C). - ^{1}H-NMR: 3.9 (s, 2H, NH_2), 4.0-4.4 (m, 4H, O-CH_2-CH_2-O); 5.8 (s, 1H, NH), 6.3 (s, 1H, CH), 7.3-8.2 (m, 4H, Ar-H); 8.5 (s, 1H, H-4); signals for NH and NH_2 are deuterium exchangeable. - $C_{12}H_{13}N_3O_2$ (231.3) Calcd. C 62.3 H 5.66 N 18.2 Found C 62.1 H 6.0 N 17.9

3-(1,3-Dioxolan-2-yl)-2-substituted thiocarbamoylhydrazinoquinolines (**5a-d**)

A solution of **4** (0.46 g, 0.002 mole) in ethanol (6 ml) was stirred with the appropriate aralkyl or aryl isothiocyanate (0.002 mole) for 30 min at room temp., the precipitate was filtered (when no precipitate was formed drops of water were added). The product was crystallized from chloroform/ethanol (2:1) (**5b** was crystallized from ethanol), Table 1. - IR: 3460-3140 (NH); 1640, 1510 (C=N, C=C); 1580; 1290; 1030; 930 (-N-C=S I, II, III, IV bands); 1250; 1170; 1150; 1065 (C-O-C). - ^{1}H-NMR of **5a**:30.0 (s, 1H, NH, deuterium exchangeable); 3.8-4.2 (m, 4H, O-CH_2-CH_2-O); 4.9 (d, 2H, J = 5 Hz; $CH_2C_6H_5$); 5.8 (s, 1H, CH); 6.8-8.2 (m, 10H, Ar-H); 10.1 and 10.2 (two s, each 1H, 2NH, deuterium exchangeable). - ^{1}H-NMR of **5b**: 3.8-4.1 (m, 4H, O-CH_2-CH_2-O); 6.0 (s, 1H, CH); 7.2-7.8 (m, 9H, Ar-H), 7.9 (s, 1H, H-4).

Table 1: 3-(1,3-Dioxolan-2-yl)-2-substituted thiocarbamoylhydrazinoquinolines **5a-d**

Comp. No.	R	Yield %	M.p. (°C)	Molecular formula	Analyses% C	H	N	S
5a	$-CH_2C_6H_5$	60	184	$C_{20}H_{20}N_4O_2S$	63.1	5.30	14.7	8.4
				(380.5)	63.5	5.5	14.5	8.2
5b	$-C_6H_5$	45	149	$C_{19}H_{18}N_4O_2S$	62.3	4.95	15.3	8.8
				(366.4)	62.3	5.1	14.9	8.5
5c	$-C_6H_4CH_3$	60	151	$C_{20}H_{20}N_4O_2S$	63.1	5.3	14.7	8.4
	(p)			(380.5)	63.4	5.6	14.5	8.1
5d	$-C_6H_4Cl$	85	120	$C_{19}H_{17}ClN_4O_2S$	56.9	4.27	14.0	8.0
	(p)			(400.9)	56.7	3.9	13.8	8.1

Table 2: 3-(1,3-Dioxolan-2-yl)-2-(3-substituted-4-phenylthiazolin-2-ylidene)hydrazinoquinolines **6a-d.**

Comp. No.	R	Yield %	M.p. (°C) cryst. solvent	Molecular formula	Analyses % Calc./Found C	H	N	S
6a	$-CH_2C_6H_5$	35	184	$C_{28}H_{24}N_4O_2S$	70.0	5.03	11.7	6.7
			$EtOH/CHCl_3$	(480.6)	69.7	5.0	11.3	7.0
6b	$-C_6H_5$	30	184	$C_{27}H_{22}N_4O_2S$	69.5	4.75	12.0	6.9
			$EtOH/CHCl_3$	(466.6)	69.2	5.0	12.0	6.5
6c	$-C_6H_4CH_3$	65	209	$C_{28}H_{24}N_4O_2S$	70.0	5.03	11.7	6.7
	(p)		EtOH	(480.6)	69.7	5.2	11.3	7.0
6d	$-C_6H_4Cl$	75	209	$C_{27}H_{21}ClN_4O_2S$	64.7	4.22	11.2	6.4
	(p)		EtOH	(501.0)	64.5	4.0	11.1	6.2

3-(1,3-Dioxolan-2-yl)-2-(3-substituted-4-phenylthiazolin-2-ylidene)hydrazinoquinolines (**6a-d**)

To a solution of **5a-d** (0.001 mole) in chloroform (5 ml), the equivalent amount of phenacyl bromide (0.2 g, 0.001 mole) was added. The mixture was stirred for 5 min and the solvent was removed by evaporation under reduced pressure. The residue was dissolved in ethanol then treated with a solution of saturated sodium acetate (20 ml). The separated product was crystallized from the proper solvent, Table 2. - IR 3320 (NH); 1625; 1610; 1580; 1555; 1510 (C=N, δ NH, C=C); 1210; 1150; 1110; 1050 (C-O-C). - ^{1}H-NMR of **6a**: 3.4 (br. s, 1H, NH exchanged by D_2O); 4.0-4.3 (m, 6H, O-CH_2-CH_2-O and -$CH_2C_6H_5$); 5.0 (s, 1H, thiazoline H-5); 6.1 (s, 1H, CH of dioxolane); 7.1-7.7 (m, 14H, Ar-H); 8.0 (s, 1H, quinoline H-4). ^{1}H-NMR of **5b**: 3.3 (br. s, 1H, NH exchanged by D_2O); 4.1-4.5 (m, 4H, O-CH_2-CH_2-O); 5.2 (s, 1H, thiazoline H-5); 6.5 (s, 1H, CH of dioxolane); 7.4-8.3 (m, 14H, Ar-H); 8.8 (s, 1H, quinoline H-4).

3-(1,3-Dioxolan-2-yl)-2-(3-substituted-5-ethoxycarbonyl-4-methylthiazolin-2-ylidene)hydrazinoquinolines (**7a, c, d**)

A solution of **5a, c, d** (0.001 mole) in absol. ethanol (5 ml) and ethyl α-chloroacetoacetate (0.17 ml, 0.0012 mole) was heated under reflux for 1 h, cooled and neutralizied with sodium acetate solution. The precipitated product was crystallized from chloroform/ethanol mixture (3:1) (**7b** was crystallized from ethanol), Table 3. - IR: 3320 (NH); 1690 (C=O); 1620; 1560; 1530 (C=N, δ NH, C=C); 1255; 1200; 1150; 1060 (C-O-C). - ^{1}H-NMR of compound **7c** ($CDCl_3/CF_3COOH$), 1.2 (t, 3H, J = 7 Hz, $CH_2\underline{CH_3}$); 2.2 (s, 3H, $-C_6H_4\underline{CH_3}$(p)); 2.3 (s, 3H, thiazoline $-CH_3$): 3.8 (s, 1H, NH, deuterium exchange); 3.9-4.2 (m, 4H, O-CH_2-CH_2-O); 4.3 (q, 2H, J = 7 Hz, -$\underline{CH_2}CH_3$); 6.0 (s, 1H, CH of dioxolane); 7.0-8.0 (m, 8H, Ar-H); 8.6 (s, 1H, quinoline H-4). - M^+ of **7a** m/z = 490.

3-(1,3-Dioxolan-2-yl)-2-(3-substituted-4-thiazolidinon-2-ylidene)hydrazinoquinolines **8a-d**

5a-d in absol. ethanol (20 ml) ethyl bromoacetate (0.17 g, 0.001 mole) and anhydrous sodium acetate (0.08 g, 0.001 mole) were heated under reflux for 20 min, concentrated and cooled. Water was then added and the formed precipitate was filtered and crystallized from chloroform/ethanol (3:1), Table 4. - IR: 3340-3160 (NH); 1715-1680 (C=O); 1640-1630; 1600-1575; 1545-1510 (C=N, δ NH, C=C); 1245-1195; 1150; 1120-1110; 1060 (C-O-C). - ^{1}H-NMR of **8d**: 3.9 (s, 2H, thiazolidinone H-5); 4.0-4.3 (m, 5H, O-CH_2-CH_2-O and NH); 6.1 (s, 1H, CH of dioxolane); 7.3-7.8 (m, 8H, Ar-H); 8.0 (s, 1H, quinoline H-4). - M^+ of **8d** m/z = 442.

Table 3: 3-(1,3-Dioxolan-2-yl)-2-(3-substituted-5-ethoxycarbonyl-4-methylthiazolin-2-ylidene)hydrazinoquinolines **7a, c, d**

Comp. No.	R	Yield %	M.p. (°C)	Molecular formula	Analyses % Calc./Found C	H	N	S
7a	$-CH_2C_6H_5$	50	199	$C_{26}H_{26}N_4O_4S$	63.7	5.34	11.4	6.5
				(490.6)	64.0	5.0	11.8	6.5
7c	$-C_6H_4CH_3$	62	159	$C_{26}H_{26}N_4O_4S$	63.7	5.34	11.4	6.5
	(p)			(490.6)	64.0	5.7	11.5	6.8
7d	$-C_6H_4Cl$	44	258	$C_{25}H_{23}ClN_4O_4S$	58.8	4.54	11.0	6.3
	(p)			(511.0)	58.5	4.5	10.7	6.1

Table 4: 3-(1,3-Dioxolan-2-yl)-2-(3-substituted-4-thiazolidinon-2-ylidene)hydrazinoquinolines **8a-d.**

Comp. No.	%	Yield %	M.o. (°C)	Molecular formula	Analyses % C	H	N	S
8a	$-CH_2C_6H_5$	50	203	$C_{22}H_{20}N_4O_3S$	62.8	4.79	13.3	7.6
				(420.49)	62.6	5.0	13.1	7.4
8b	$-C_6H_5$	50	197	$C_{21}H_{18}N_4O_3S$	62.1	4.46	13.8	7.9
				(406.46)	62.4	4.6	13.5	7.8
8c	$-C_6H_4CH_3$ (p)	50	210	$C_{22}H_{20}N_4O_3S$	62.8	4.79	13.3	7.6
				(420.49)	62.6	5.0	13.2	7.8
8d	$-C_6H_4Cl$ (p)	60	217	$C_{21}H_{17}ClN_4O_3S$	57.2	3.89	12.7	7.3
				(440.91)	57.0	4.1	12.8	6.9

Table 5: 3-(1,3-Dioxolan-2-yl)-2-(3-substituted-5-arylidene-4-thiazolidinon-2-ylidene)hydrazinoquinolines **9a-i**

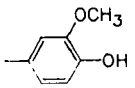
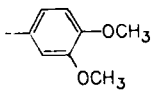
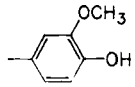
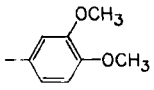
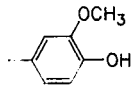
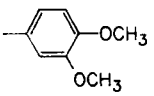
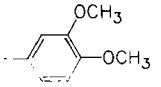
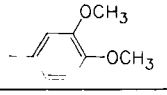
Comp. No.	R	R^1	Yield %	M.p. (°C) Cryst. Solv.	Molecular formula	Analyses % Calc./Found C	H	N	S
9a	$-C_6H_5$	$-C_6H_5$	36	195 EtOH	$C_{28}H_{22}N_4O_3S$ (494.6)	68.0 / 68.3	4.48 / 4.7	11.3 / 11.0	6.5 / 6.7
9b	$-C_6H_5$		41	220 EtOH	$C_{29}H_{24}N_4O_5S$ (540.6)	64.4 / 64.7	4.47 / 4.7	10.4 / 10.0	5.9 / 6.2
9c	$-C_6H_5$		32	200 EtOH	$C_{30}H_{26}N_4O_5S$ (554.6)	65.0 / 64.8	4.72 / 4.9	10.1 / 9.8	5.8 / 5.5
9d	$-C_6H_4CH_3$ (p)	$-C_6H_5$	33	200 EtOH	$C_{29}H_{24}N_4O_3S$ (508.6)	68.5 / 68.6	4.76 / 4.8	11.0 / 11.0	6.3 / 6.0
9e	$-C_6H_4CH_3$ (p)		61	189 Dioxane	$C_{30}H_{26}N_4O_5S$ (554.6)	65.0 / 64.6	4.72 / 4.5	10.1 / 10.0	5.8 / 5.5
9f	$-C_6H_4CH_3$ (p)		41	221 Dioxane	$C_{31}H_{28}N_4O_5S$ (568.6)	65.5 / 65.8	4.96 / 4.8	9.9 / 9.7	5.6 / 6.0
9g	$-C_6H_4Cl$ (p)	$-C_6H_5$	28	220 $CHCl_3$	$C_{28}H_{21}ClN_4O_3S$ (529.0)	63.6 / 63.2	4.00 / 4.3	10.6 / 10.3	6.1 / 6.3
9h	$-C_6H_4Cl$ (p)		46	160 Benzene	$C_{29}H_{23}ClN_4O_5S$ (575.0)	60.6 / 60.2	4.03 / 4.3	9.7 / 9.5	5.6 / 5.7
9i	$-C_6H_4Cl$ (p)		42	125 MeOH/$CHCl_3$	$C_{30}H_{25}ClN_4O_5S$ (589.1)	61.2 / 61.1	4.28 / 4.2	9.5 / 9.2	5.4 / 5.3

Table 6: 2-(3-Substituted-4-thiazolidinon-2-ylidene)hydrazinoquinoline-3-carbaldehydes **10a-d.**

Comp. No.	R	Yield %	M.p. (°C)	Molecular formula	Analyses % Calc./Found C	H	N	S
10a	$-CH_2C_6H_5$	53	120	$C_{20}H_{16}N_4O_2S$	63.8	4.28	14.9	8.5
				(376.4)	63.5	4.4	14.9	8.2
10b	$-C_6H_5$	49	210	$C_{19}H_{14}N_4O_2S$	63.0	3.89	15.5	8.9
				(362.4)	62.6	4.0	15.2	9.0
10c	$-C_6H_4CH_3$ (p)	50	199	$C_{20}H_{16}N_4O_2S$	63.8	4.28	14.9	8.5
				(376.4)	63.5	4.2	15.0	8.7
10d	$-C_6H_4Cl$ (p)	50	116	$C_{19}H_{13}ClN_4O_2S$	57.5	3.30	14.1	8.1
				(396.9)	57.4	3.5	14.4	7.9

Table 7: 2-(3-Substituted-5-arylidene-4-thiazolidinon-2-ylidene)hydrazinoquinoline-3-carbaldehydes **11a-d**.

Comp. No.	R	R^1	Yield* %	M.p. (°C)	Molecular formula	Analyses % Calc./Found C	H	N	S
11a	$-C_6H_4CH_3$ (p)	$-C_6H_5$	40	131	$C_{27}H_{20}N_4O_2S$ (464.5)	69.8 / 69.7	4.34 / 4.2	12.1 / 12.4	6.9 / 7.0
11b	$-C_6H_4CH_3$ (p)		35	228	$C_{29}H_{24}N_4O_4S$ (524.6)	66.4 / 66.0	4.61 / 4.4	10.7 / 10.5	6.1 / 6.0
11c	$-C_6H_4Cl$ (p)	$-C_6H_5$	40	143	$C_{26}H_{17}ClN_4O_2S$ (485.0)	64.4 / 64.4	3.53 / 3.3	11.5 / 11.7	6.6 / 6.8
11d	$-C_6H_4Cl$ (p)		36	105	$C_{28}H_{21}ClN_4O_4S$ (545.0)	61.7 / 61.5	3.88 / 3.5	10.3 / 10.4	5.9 / 5.6

* The yield was based on method II.

3-(1,3-Dioxolan-2-yl)-2-(3-substituted-5-arylidene-4-thiazolidinon-2-ylidene)hydrazinoquinolines (**9a-i**)

A mixture of the proper **8b-d** (0.001 mole) in 5 ml of dioxane/methanol mixture (1:3), the selected aldehyde (benzaldehyde, vanillin, or veratraldehyde) (0.003 mole) and triethylamine (1 ml) was heated under reflux for the specified time (for phenyl or p-chloro derivatives from 8-12 h and for p-tolyl 25-35 h). The mixture was filtered and the product was crystallized from the proper solvent, Table 5. - IR: 3460-3140 (NH); 1695-1680 (C=O); 1630; 1615-1605; 1595-1585; 1545-1530 (C=N, δ NH, C=C); 1250; 1150; 1120-1110; 1070 (C-O-C). - ^{1}H-NMR of compound **9f**: 2.5 (s, 3H, $C_6H_4CH_3$(p)), 3.9 (s, 6H, 2-OCH_3); 3.3 (s, 1H, NH, deuterium exchange); 4.0-4.2 (m, 4H, O-CH_2-CH_2-O); 6.2 (s, 1H, CH of dioxolane); 6.8-8.2 (m, 13H, Ar-H, N=CH-R). - M^+ of **9a** m/z = 494. - M^+ of **9g** m/z = 528.

2-(3-Substituted-4-thiazolidinon-2-ylidene)hydrazinoquinoline-3-carbaldehydes (**10a-d**)

A solution of **8a-d** (0.001 mole) in glacial acetic acid (5 ml) was heated under reflux for 1 h. The mixture was concentrated, cooled and poured into water (20 ml). The formed precipitate was washed with water and crystallized from aqueous ethanol (1:4) (**10d** was crystallized from ethyl acetate), Table 6. - IR: 3360-3140 (NH); 1720-1700 (C=O, aldehyde); 1680-1670 (C=O, thiazolidinone); 1650-1630; 1600-1595; 1560-1530 (C=N, δ NH, C=C).

2-(3-Substituted-5-arylidene-4-thiazolidinon-2-ylidene)hydrazinoquinoline-3-carbaldehydes (**11a-d**)

Method I: A solution of **9d, f, g, i** (0.001 mole) in glacial acetic acid (5 ml) was heated under reflux for 1 h. The reaction mixture was cooled and poured into water (20 ml). The formed precipitate was washed with water and crystallized from aqueous ethanol, Table 7.

Method II: To a solution of **10c** or **d** (0.001 mole) in ethanol (5 ml) benzaldehyde or veratraldehyde (0.001 mole) and triethylamine (0.05 ml) were added. The mixture was heated under reflux for 2 h cooled, the obtained crystalline precipitate was filtered and crystallized from ethanol, Table 7. - IR: 3340 (NH); 1700 (C=O, aldehyde); 1680 (C=O, thiazolidinone); 1630; 1600; 1530; 1510 (C=N, δ NH, C=C).

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