Chemistry of Substituted Quinolinones
I. Synthesis of Novel Triazinylmethylquinolinone Derivatives

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Functionalization of 1*H*-quinolin-2-one moiety, at the position 3, with pyruvic or 2-thiopyruvic acid substrates, in order to develop novel synthons of heterocyclic derivatives of quinolinone, was achieved through ring-closure and ring-opening routes. The syntheses of some new 3-([1,2,4]triazin-6-ylmethyl)quinolines have been described. Three multiaza-polynuclear heterocycles, *viz.* triazinophthalazine, triazinoindole, and bistriazinoquinoxaline, were also synthesized and are expected to have biological importance. The structures of all new products were verified on the basis of their elemental and spectral analyses.

Within the framework of research related to synthesis and reactions of 4-hydroxy-1*H*-quinolin-2-ones [1—4], we herein report the synthesis of novel functionally substituted quinolinones. 4-Hydroxy-1*H*-quinolin-2-ones represent one of the most important classes of heterocycles, possessing a wide spectrum of biological activities [5—10]. Also, [1,2,4]triazin-5-ones are well known to exhibit diverse pharmacological actions [11—14]. So that it is thought that if both quinolinone and triazinone moieties are combined in one molecular frame, the possible products might have considerable biological potencies.

4-Hydroxy-8-methyl-1*H*-quinolin-2-one (*I*) was prepared following a method similar to that described in Ref. [15], and formylated by the Reimer—Tiemann reaction, giving 3-formyl-4-hydroxy-8-methyl-1*H*-quinolin-2-one (*II*). The reaction of the aldehyde *II* with hippuric acid in the presence of sodium acetate did not lead to the expected oxazolin-5-one derivative, instead 3-benzoylamino-7-methyl-5,6-dihydro-2*H*-pyrano[3,2-*c*]quinoline-2,5-dione (*III*) was produced. The structure of compound *III* was elucidated by its elemental analysis, IR and ^{1}H NMR spectral data, which revealed the involvement of the O—H group in an intramolecular cyclization. This cyclization may take place as a consequent step after condensation of the CHO group with the active methylene of hippuric acid. We have obtained similar results in an earlier work [1]. It was found that pyranoquinoline *III* underwent ring-opening, when treated with aqueous sodium hydroxide solution, to give 2-benzoylamino-3-(1,2-dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)acrylic acid (*IV*), which in its ^{1}H NMR spectrum revealed two additional signals at δ = 11.61 and 13.74 due to two protons (phenolic and carboxylic) exchangeable with deuterium on treating with deuterium oxide. Moreover, acid hydrolysis of the acrylic acid derivative *IV* furnished 3-(1,2-dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)pyruvic acid (*V*), which was utilized, hereafter, as a synthon for some new triazinylmethylquinolines. The mass spectrum of compound *V* showed a molecular ion peak at *m/z* (I_r/%): 261 (20), accompanied by an (M + 1) ion peak at *m/z* (I_r/%): 262 (3), confirming the proposed structural formula of this compound (Scheme 1).

In order to obtain 2-thiopyruvic acid derivative *VIII*, as the thio-isomer of compound *V*, condensation of the aldehyde *II* with 2-phenyliminothiazolidin-4-one (*VI*) was carried out, in the presence of fused sodium acetate. 5-(1,2-Dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)methylene-2-phenyliminothiazolidin-4-one (*VII*), product of the latter reaction, was subjected to an exhaustive alkaline hydrolysis to afford 3-(1,2-dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)-2-thiopyruvic acid (*VIII*). The structure of compound *VIII* was verified from its mass spectrum, which revealed a molecular ion peak at *m/z* (I_r/%): 277 (9) along with an (M + 1) ion peak at *m/z* (I_r/%): 278 (1). Beside the analytical and spectral evidences for the structure *VIII*, it found a good chemical proof by its independent synthesis through the condensation of aldehyde *II* with 2-sulfanylacetic acid (Scheme 2).

Reaction of the pyranoquinoline *III* with hydrazine

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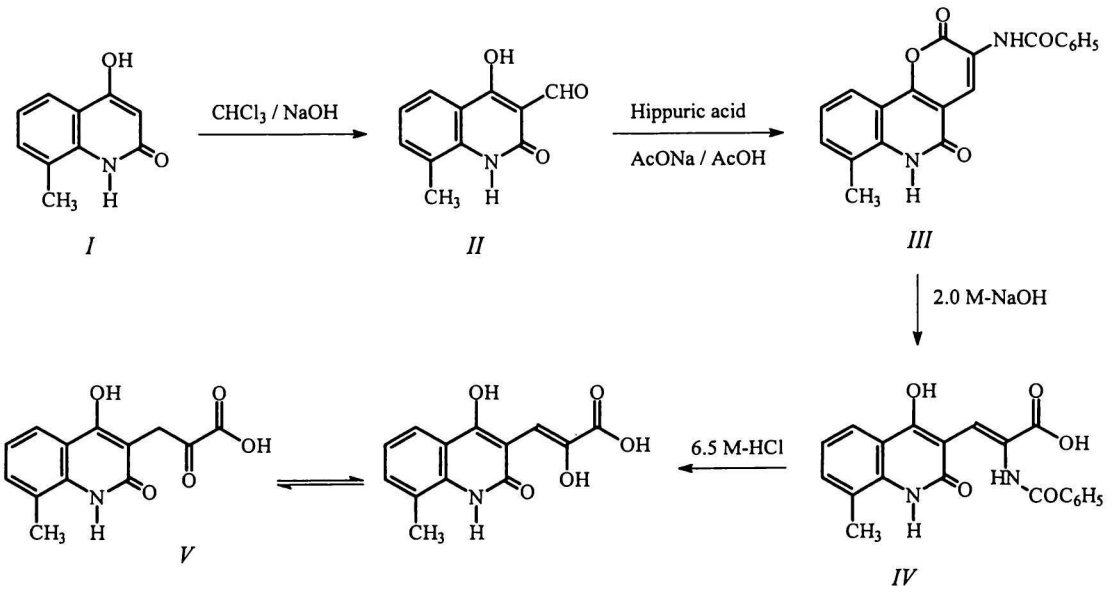
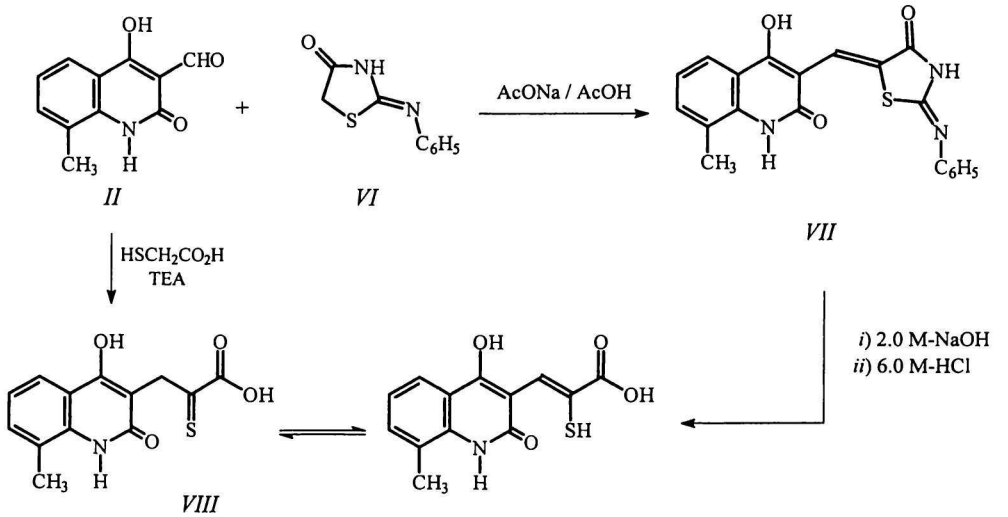


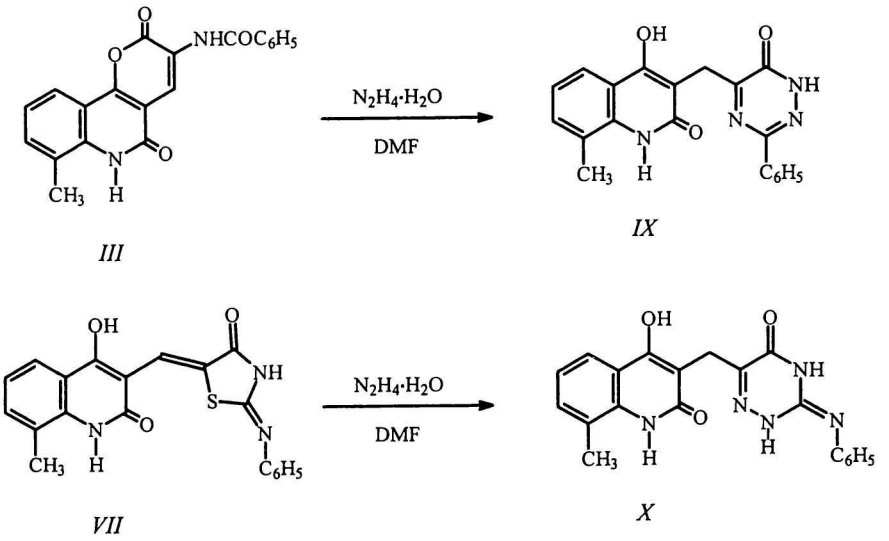
Scheme 1



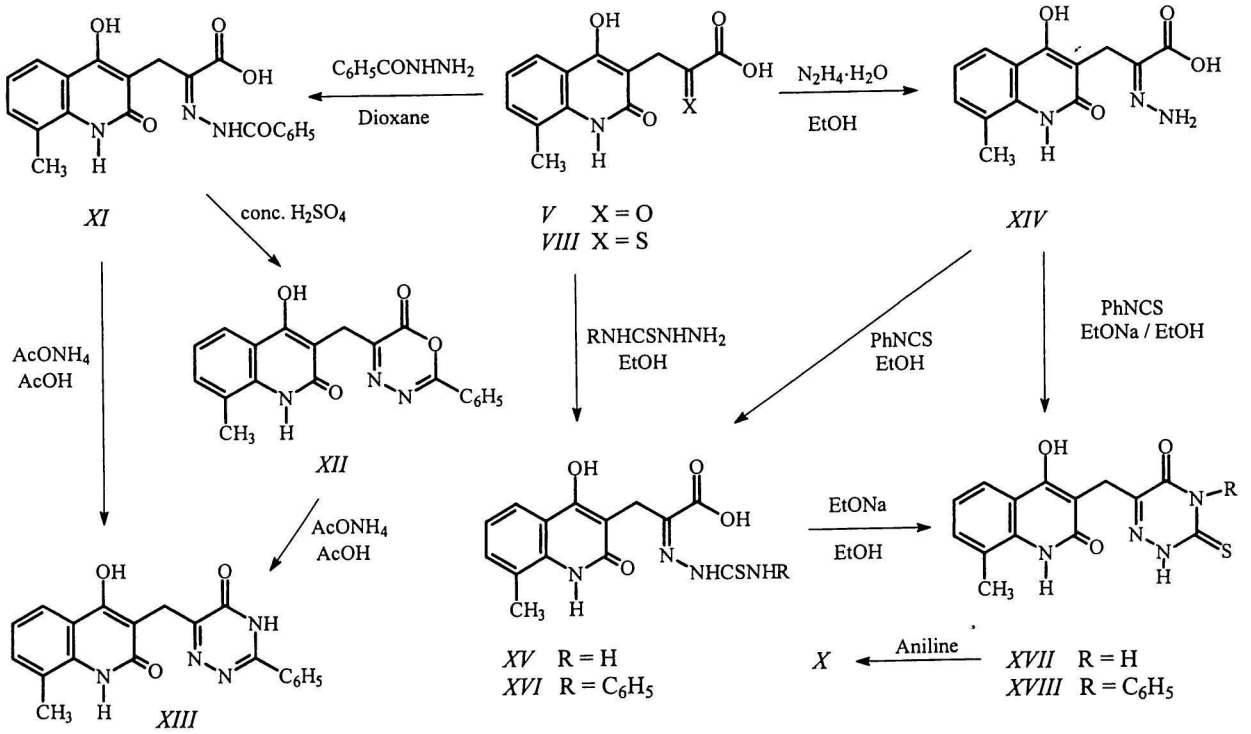
Scheme 2

hydrate in DMF caused successive ring-opening and ring-closure transformations to give 3-(1,6-dihydro-6-oxo-3-phenyl[1,2,4]triazin-5-yl)methyl-4-hydroxy-8-methyl-1*H*-quinolin-2-one (*IX*). The structure of this product was supported by the presence of a phenolic OH group, and also by the absence of both carboxylic and amino groups, as it is indicated in its IR and ^{1}H NMR spectra. Similarly, heating the quinolinylmethylenethiazolidine *VII* with hydrazine hydrate gave 4-hydroxy-8-methyl-3-(5-oxo-3-phenylimino-2,3,4,5-tetrahydro[1,2,4]triazin-6-yl)methyl-1*H*-quinolin-2-one (*X*). ^{1}H NMR spectrum of compound *X* revealed four different singlet signals corresponding to four deuterium exchangeable protons of three (N—H) groups, and one more downfield shifted (O—H) group (Scheme 3).

Condensation of equimolar amounts of either the pyruvic acid *V* or 2-thiopyruvic acid *VIII* with benzoic hydrazide afforded one and the same product. It was found that condensation reaction took place at the α-oxo (or α-thioxo) group of the pyruvic acid side chain, giving rise to 3-(1,2-dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)pyruvic acid 2-benzoylhydrazone (*XI*). On stirring the benzoylhydrazone derivative with concentrated sulfuric acid, 4-hydroxy-8-methyl-3-(6-oxo-2-phenyl[1,3,4]oxadiazin-5-yl)methyl-1*H*-quinolin-2-one (*XII*) was obtained. Treating the oxadiazinylmethylquinoline *XII* with ammonium acetate in boiling acetic acid furnished 3-(4,5-dihydro-5-oxo-3-phenyl[1,2,4]triazin-6-yl)methyl-4-hydroxy-8-methyl-1*H*-quinolin-2-one (*XIII*), an isomer of the compound *IX*. Also, the compound *XIII*



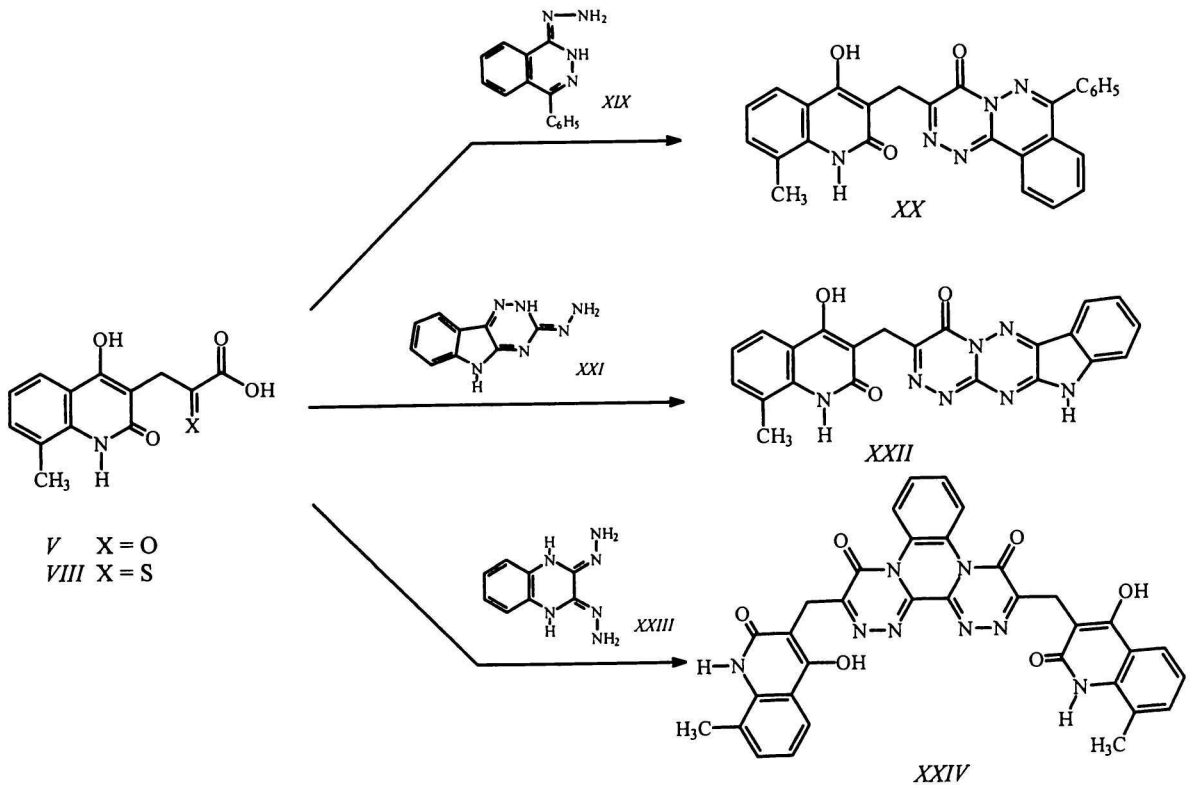
Scheme 3



Scheme 4

was directly obtained from reaction of ammonium acetate and the 2-benzoylhydrazone *XI*.

Treatment of either *V* or *VIII* with hydrazine hydrate resulted in the same condensation product, 3-(1,2-dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)-pyruvic acid 2-hydrazone (*XIV*). The structure of *XIV* was emphasized by its elemental and spectral analyses. In addition, when compound *XIV* was reacted with phenyl isothiocyanate in ethanol, 3-(1,2-dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)pyruvic acid 2-(4-phenylthiosemicarbazone) (*XVI*) was obtained. Alternatively, the resultant *XVI* was easily prepared from the condensation of 4-phenylthiosemicarbazide with the pyruvic acid derivative *V* in ethanol. By the same manner, 3-(1,2-dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)pyruvic acid 2-thiosemicarbazone (*XV*) was obtained from condensation of *V* and thiosemicarbazide. Each of compounds *XV* and *XVI* underwent ring-closure reaction when they were cured with sodium ethoxide in boiling ethanol, furnishing 4-hydroxy-8-methyl-3-(5-oxo-3-thioxo-2,3,4,5-tetrahydro[1,2,4]triazin-6-yl)methyl-1*H*-quinolin-2-ones *XVII*



Scheme 5

(R = H) and *XVIII* (R = Ph), respectively. Moreover, when the hydrazone *XIV* was reacted with phenyl isothiocyanate in the presence of sodium ethoxide, compound *XVIII* was attained. Beside the spectral evidences for the structures of the latter two products, it was found that the reaction of aniline with *XVII* led to the replacement of the thioxo group to give the previously obtained phenyliminotriazinylmethylquinoline *X* (Scheme 4).

It was intended that the reaction of the pyruvic acid *V* and/or its thio-isomer *VIII* with α-hydrazino-*N*-heterocycles might result in some new multiaza-polynuclear systems of expected biological importance. Thus, compounds *V* and/or *VIII* were subjected to react with 1-hydrazono-4-phenylphthalazine (*XIX*) [16] in boiling DMF, affording 3-(1,2-dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)methyl-4-oxo-7-phenyl[1,2,4]triazino[3,4-*a*]phthalazine (*XX*). Its mass spectrum showed a molecular ion peak at *m/z* (I_r/%): 461 (16), accompanied by an (M + 1) ion peak at *m/z* (I_r/%): 462 (4), supporting the suggested proposal of its molecular formula. Similarly, the reaction of *V* and/or *VIII* with 3-hydrazono[1,2,4]triazino[5,6-*b*]indole (*XXI*) [17] gave a linear condensed system, identified as 3-(1,2-dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)methyl-4-oxo[1,2,4]triazino[4′,3′:2,3][1,2,4]triazino[5,6-*b*]indole (*XXII*). Spectral characterization of compound *XXII* indicated that the carboxylic group is no longer present, as well as the hydrazono group. Molecular ion peak appeared at *m/z* (I_r/%): 425 (13), accompanied by an (M + 1) ion peak at *m/z* (I_r/%): 426 (3), and the base peak at *m/z* 187, corresponding to the 2,4-dioxo-8-methyl-3-methylenequinolinium ion $[C_{11}H_9NO_2]^+$.

Finally, when *V* and/or *VIII* were heated with 2,3-bishydrazonoquinoxaline (*XXIII*) [18] in DMF, 2,7-bis((1,2-dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)methyl)-1,8-dioxo-bis[1,2,4]triazino[4,3-*a*;3′,4′-*c*]-quinoxaline (*XXIV*) was obtained. The elemental and spectroscopic data are in good agreement with the proposed structure of compound *XXIV*. ^{1}H NMR spectrum of *XXIV* showed duplicated integration of the characteristic 4-hydroxy-8-methyl-1*H*-quinolin-2-one moiety protons, along with four methylene protons at δ = 3.85, while the integration of the proton signals corresponding to the aromatic protons region indicated that ten aromatic protons were present (Scheme 5).

EXPERIMENTAL

Melting points were determined in open capillary tubes on a Gallenkamp MFB-595 apparatus, and are uncorrected. IR spectra were recorded on a Perkin—Elmer FT-IR 1650 spectrophotometer, using samples in KBr discs. ^{1}H NMR spectra were measured on a Jeol FX-90 spectrometer (90 MHz), using DMSO-d_6 as solvent and TMS as internal standard. Mass spectra were obtained on a Hewlett—Packard MS-5988 by direct inlet (electron energy 70 eV). Elemental mi-

Table 1. Characterization of the New Compounds *I*—*XXIV*

Compound	Formula M_r	w_i(calc.)/% w_i(found)/%			Yield	M.p.	Solvent
		C	H	N	%	°C	
I	$C_{10}H_9NO_2$	68.56	5.15	8.00	72	> 300	DMF
	175.06	68.40	4.85	7.80			
II	$C_{11}H_9NO_3$	65.02	4.43	6.90	64	> 300	AcOH
	203.06	64.75	4.40	6.65			
III	$C_{20}H_{14}N_2O_4$	69.36	4.05	8.09	83	> 300	DMF
	346.09	69.10	4.20	8.30			
IV	$C_{20}H_{16}N_2O_5$	65.93	4.40	7.69	80	> 300	BuOH
	364.11	65.55	4.30	7.90			
V	$C_{13}H_{11}NO_5$	59.77	4.21	5.36	86	> 300	DMF
	261.06	59.40	4.05	5.40			
VII	$C_{20}H_{15}N_3O_3S$	63.66	3.98	11.14	75	243	AcOH
	377.08	63.60	3.95	11.40			
VIII	$C_{13}H_{11}NO_4S$	56.32	3.97	5.05	68[a]	224	AcOH
	277.04	56.10	4.10	5.20	43[b]		
IX	$C_{20}H_{16}N_4O_3$	66.67	4.44	15.56	62	> 300	Dioxane
	360.12	66.45	4.30	15.30			
X	$C_{20}H_{17}N_5O_3$	64.00	4.53	18.67	60[a]	> 300	DMF
	375.13	63.80	4.80	18.60	45[b]		
XI	$C_{20}H_{17}N_3O_5$	63.32	4.49	11.08	64	> 300	DMF
	379.12	63.40	4.50	11.20			
XII	$C_{20}H_{15}N_3O_4$	66.48	4.16	11.63	53	> 300	AcOH
	361.11	66.25	4.30	11.40			
XIII	$C_{20}H_{16}N_4O_3$	66.67	4.44	15.56	57[a]	> 300	AcOH
	360.12	66.75	4.50	15.30	70[b]		
XIV	$C_{13}H_{13}N_3O_4$	56.71	4.71	15.27	86	> 300	EtOH/H_2O
	275.09	56.75	4.60	15.10			
XV	$C_{14}H_{14}N_4O_4S$	50.30	4.19	16.77	83	> 300	*iso*-PrOH
	334.07	50.25	4.30	16.50			
XVI	$C_{20}H_{18}N_4O_4S$	58.54	4.39	13.66	92[a]	> 300	DMF
	410.10	58.30	4.10	13.50	85[b]		
XVII	$C_{14}H_{12}N_4O_3S$	53.16	3.80	17.72	60[a]	> 300	DMF
	316.06	53.40	4.05	17.50			
XVIII	$C_{20}H_{16}N_4O_3S$	61.22	4.08	14.29	62[a]	> 300	AcOH
	392.09	61.30	4.20	14.00	68[b]		
XX	$C_{27}H_{19}N_5O_3$	70.28	4.12	15.18	78	> 300	DMSO
	461.15	70.20	4.40	15.35			
XXII	$C_{22}H_{15}N_7O_3$	62.12	3.53	23.06	69	> 300	DMSO
	425.12	62.45	3.65	23.20			
XXIV	$C_{34}H_{24}N_8O_6$	63.75	3.75	17.50	74	> 300	TFA
	640.18	63.80	3.60	17.40			

a), *b*) Preparation methods *a* and *b*, respectively.

croanalyses were performed at the Cairo University Microanalytical Centre. Analytical data are given in Table 1.

4-Hydroxy-8-methyl-1*H*-quinolin-2-one (*I*)

A mixture of 2-toluidine (0.3 mol; 32.3 cm^3) and diethyl malonate (0.36 mol; 55.2 cm^3) was treated with freshly prepared polyphosphoric acid (138 g) and heated at 180—190 °C for 1 h. Then the temperature was raised gradually to 220 °C for an additional 1 h and the mixture was poured onto crushed ice. The formed crude solid was dissolved in aqueous sodium hydroxide (500 cm^3, 2.0 M-NaOH), extracted with benzene (4 × 100 cm^3), active charcoal (50 g) was added, and then the solution was filtered. The clear filtrate was acidified with hydrochloric acid (170 cm^3, 6.0 M-HCl), the solid was collected by filtration, washed with water (5 × 100 cm^3), and crystallized. IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$: 752, 803, 1182, 1244, 1365, 1468, 1507, 1606 ν(C=C), 1661 ν(C=O), 2500—3280 ν(N—H and O—H). ^{1}H NMR spectrum (DMSO-d_6), δ: 1.83 (s, 3H, CH_3), 6.02 (s, 1H, C-3—H), 7.25—7.70 (m, 3H, H_{arom}), 10.37 (s, 1H, N—H), 11.45 (s, 1H, O—H).

3-Formyl-4-hydroxy-8-methyl-1*H*-quinolin-2-one (*II*)

To a suspension of compound *I* (0.1 mol), in chloroform (225 cm^3) aqueous sodium hydroxide (1200 cm^3, 4.0 M-NaOH) was added and the mixture was gently boiled under reflux for 6 h. Excess chloroform was then evacuated, and the solid, that deposited, was filtered,

washed with methanol (50 cm^3), and stirred with hydrochloric acid (400 cm^3, 6.0 M-HCl). The formed amber yellow precipitate was filtered off, washed with water, and crystallized. IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$: 762, 802, 1071, 1186, 1352, 1460, 1564, 1602 ν(C=C), 1642 $\nu(C{=}O_{quinolone})$, 1678 $\nu(C{=}O_{formyl})$, 2730, 2886 $\nu(C{-}H_{formyl})$, 3175 ν(N—H and O—H). ^{1}H NMR spectrum (DMSO-d_6), δ: 1.85 (s, 3H, CH_3), 7.32—7.85 (m, 3H, H_{arom}), 9.28 (s, 1H, H_{formyl}), 10.96 (s, 1H, N—H), 11.58 (s, 1H, O—H).

3-Benzoylamino-7-methyl-5,6-dihydro-2*H*-pyrano[3,2-*c*]quinoline-2,5-dione (*III*)

A mixture of the formyl derivative *II* (0.05 mol), hippuric acid (0.05 mol), anhydrous sodium acetate (0.15 mol), and glacial acetic acid (100 cm^3) was heated under reflux for 4 h. The resulting canary-yellow solid was collected by filtration, washed thoroughly with cold methanol (20 cm^3), and crystallized. IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$: 775, 800, 1103 ν(C—O—C), 1247, 1284, 1522, 1566, 1607 ν(C=C), 1644 $\nu(C{=}O_{quinolone})$, 1696 $\nu(C{=}O_{benzamide})$, 1733 $\nu(C{=}O_{pyranone})$, 3171—3372 ν(N—H). ^{1}H NMR spectrum (DMSO-d_6), δ: 1.82 (s, 3H, CH_3), 7.29—7.82 (m, 9H, H_{arom} + C-3—H), 10.37 (s, 1H, $N{-}H_{quinolone}$), 10.92 (s, 1H, $N{-}H_{benzamide}$).

2-Benzoylamino-3-(1,2-dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)acrylic Acid (*IV*)

The pyranoquinoline *III* (0.03 mol) was treated with aqueous sodium hydroxide (100 cm^3, 2.0 M-NaOH) and the mixture was boiled under reflux for 2 h, then filtered while hot. The filtrate was acidified with hydrochloric acid (30 cm^3, 6.0 M-HCl) and the formed solid was filtered off. The crude material was purified by dissolution in aqueous sodium carbonate (100 cm^3, 1.0 M-Na_2CO_3), reprecipitated using hydrochloric acid (30 cm^3, 6.0 M-HCl), and then crystallized. IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$: 1029, 1228, 1452, 1506, 1586, 1600 ν(C=C), 1648 $\nu(C{=}O_{quinolone})$, 1686 $\nu(C{=}O_{benzamide})$, 1725 $\nu(C{=}O_{carboxylic})$, 2596—3168 ν(N—H and O—H). ^{1}H NMR spectrum (DMSO-d_6), δ: 1.78 (s, 3H, CH_3), 6.26 (s, 1H, H_{olefin}), 7.25—7.76 (m, 8H, H_{arom}), 10.17 (s, 1H, $N{-}H_{quinolone}$), 11.00 (s, 1H, $N{-}H_{benzamide}$), 11.61 (s, 1H, $O{-}H_{quinolinol}$), 13.74 (s, 1H, $O{-}H_{carboxylic}$).

3-(1,2-Dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)pyruvic Acid (*V*)

A suspension of compound *IV* (0.02 mol) in ethanol (50 cm^3) was treated with hydrochloric acid (50 cm^3, 6.0 M-HCl) and refluxed for 2 h. The reaction mixture was filtered while hot, washed with water, and crystallized. IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$: 1124, 1450, 1570, 1600 ν(C=C), 1637 $\nu(C{=}O_{quinolone})$, 1669 $\nu(C{=}O_{keto})$, 1725 $\nu(C{=}O_{carboxylic})$, 2560—3360 ν(N—H and O—H). ^{1}H NMR spectrum (DMSO-d_6), δ: 1.86 (s, 3H, CH_3), 4.20 (s, 2H, CH_2CO), 7.25—7.78 (m, 3H, H_{arom}), 10.15 (s, 1H, $N{-}H_{quinolone}$), 11.45 (s, 1H, $O{-}H_{quinolinol}$), 13.42 (s, 1H, $O{-}H_{carboxylic}$). Mass spectrum, m/z (I_r/%): 262 (3, $[M + 1]^+$), 261 (20, $[M]^+$), 243 (66, $[M - H_2O]^+$), 217 (50, $[M - CO_2]^+$), 216 (43), 215 (84), 189 (21), 188 (100), 187 (81), 175 (65), 160 (11), 159 (11), 157 (10), 147 (17), 134 (40), 133 (14), 131 (12), 130 (32), 129 (20), 106 (25), 105 (46), 91 (34), 90 (15), 65 (19).

5-(1,2-Dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)methylene-2-phenyliminothiazolidin-4-one (*VII*)

The formyl derivative *II* (0.05 mol) was dissolved in glacial acetic acid (150 cm^3), containing anhydrous sodium acetate (0.15 mol), and treated with 2-phenyliminothiazolidin-4-one *VI* (0.05 mol). The reaction mixture was heated under reflux for 4 h, then cooled and the formed deposit was filtered off, washed thoroughly with ethanol (3 × 10 cm^3), and crystallized. IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$: 778, 805, 1175, 1288 ν(N—C=S), 1367, 1524, 1592, 1624 ν(C=N), 1647 $\nu(C{=}O_{quinolone})$, 1668 $\nu(C{=}O_{thiazolidinone})$, 3172—3320 ν(N—H and O—H). ^{1}H NMR spectrum (DMSO-d_6), δ: 1.81 (s, 3H, CH_3), 6.87 (s, 1H, H_{olefin}), 7.26—7.87 (m, 8H, H_{arom}), 10.62 (s, 1H, $N{-}H_{quinolone}$), 10.94 (s, 1H, $N{-}H_{thiazolidinone}$), 11.42 (s, 1H, O—H).

3-(1,2-Dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)-2-thiopyruvic Acid (*VIII*)

a) Aqueous sodium hydroxide solution (100 cm^3, 2.0 M-NaOH) was added to finely powdered *VII* (0.02 mol), and heated under reflux for 2.5 h. The reaction mixture was then cooled, diluted with cold water (100 cm^3), and filtered. The clear filtrate was treated with hydrochloric acid (35 cm^3, 6.0 M-HCl) and the formed precipitate was filtered off, washed and then crystallized. IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$: 1191, 1272 ν(C=S), 1395, 1450, 1548, 1588—1605 ν(C=C), 1641 $\nu(C{=}O_{quinolone})$, 1728 $\nu(C{=}O_{carboxylic})$, 2560—3300 ν(N—H and O—H). ^{1}H NMR spectrum (DMSO-d_6), δ: 1.83 (s, 3H, CH_3), 4.56 (s, 2H, CH_2CS), 7.20—7.65 (m, 3H, H_{arom}), 10.33 (s, 1H, $N{-}H_{quinolone}$), 11.56 (s, 1H, $O{-}H_{quinolinol}$), 13.48 (s, 1H, $O{-}H_{carboxylic}$). Mass spectrum, m/z (I_r/%): 278 (1, $[M + 1]^+$), 277 (9, $[M]^+$), 259 (12, $[M - H_2O]^+$), 233 (3, $[M - CO_2]^+$), 232 (10), 231 (11), 190 (2), 188 (100), 187 (92), 175 (15), 160 (12), 159 (12), 147 (13), 133 (9), 131 (12), 119 (39), 105 (15), 93 (94), 90 (5), 77 (36), 65 (45).

b) The formyl derivative *II* (0.01 mol) and 2-sulfanylacetic acid (0.12 mol) in absolute ethanol (100 cm^3) were boiled in the presence of triethylamine (0.2

cm^3) for 4 h. The mixture was then filtered off, the afforded filtrate was acidified with hydrochloric acid (2 cm^3, 6.0 M-HCl), and the deposits were collected by filtration, crystallized, and identified by its melting point, mixed melting point, and spectral data.

3-(1,6-Dihydro-6-oxo-3-phenyl[1,2,4]triazin-5-yl)methyl-4-hydroxy-8-methyl-1*H*-quinolin-2-one (*IX*)

The pyranoquinoline *III* (5 mmol) was boiled with hydrazine hydrate (7 mmol, w = 100 %) in DMF (25 cm^3) for 6 h. Afterwards, the mixture was cooled, the obtained crystalline deposits were filtered off, and recrystallized. IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$: 1446, 1565, 1587, 1605 ν(C=C), 1620 ν(C=N), 1648 $\nu(C{=}O_{quinolone})$, 1674 $\nu(C{=}O_{triazinone})$, 2720—3167 ν(N—H and O—H). ^{1}H NMR spectrum (DMSO-d_6), δ: 1.82 (s, 3H, CH_3), 3.85 (s, 2H, CH_2), 7.30—7.83 (m, 8H, H_{arom}), 10.60 (s, 1H, $N{-}H_{quinolone}$), 10.81 (s, 1H, $N{-}H_{triazinone}$), 11.32 (s, 1H, O—H).

4-Hydroxy-8-methyl-3-(5-oxo-3-phenylimino-2,3,4,5-tetrahydro[1,2,4]triazin-6-yl)methyl-1*H*-quinolin-2-one (*X*)

a) The compound *VII* (5 mmol) and hydrazine hydrate (5 mmol, w = 100 %) in DMF (25 cm^3) were refluxed for 5 h. Then the mixture was cooled and poured onto crushed ice. The obtained precipitate was filtered off and crystallized. IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$: 1449, 1570, 1604 ν(C=C), 1612—1620 ν(C=N), 1641 $\nu(C{=}O_{quinolone})$, 1680 $\nu(C{=}O_{triazinone})$, 3086—3344 ν(N—H and O—H). ^{1}H NMR spectrum (DMSO-d_6), δ: 1.80 (s, 3H, CH_3), 3.86 (s, 2H, CH_2), 7.27—7.85 (m, 8H, H_{arom}), 10.30 (s, 1H, N-2—$H_{triazinone}$), 10.62 (s, 1H, $N{-}H_{quinolone}$), 10.85 (s, 1H, N-4—$H_{triazinone}$), 11.35 (s, 1H, O—H).

b) A mixture of compound *XVII* (2 mmol), anilinium chloride (2 mmol), and aniline (5 cm^3) was heated under reflux for 10 h. The reaction mixture was then cooled and triturated with methanol (25 cm^3). The obtained solid was filtered off, washed with diethyl ether (3 × 20 cm^3), crystallized, and identified by its melting point, mixed melting point, and spectral data.

3-(1,2-Dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)pyruvic Acid 2-Benzoylhydrazone (*XI*)

A mixture of either *V* or *VIII* (5 mmol) and benzoic hydrazide (5 mmol) in dioxane (30 cm^3) was heated under reflux for 2 h. Then, the obtained solid precipitate was filtered off while hot and crystallized. IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$: 776, 1188, 1326, 1550, 1573, 1611 ν(C=N), 1633, 1645 $\nu(C{=}O_{quinolone})$, 1682 $\nu(C{=}O_{benzoyl})$, 1725 $\nu(C{=}O_{carboxylic})$, 2620—3205 ν(N—H and O—H). ^{1}H NMR spectrum (DMSO-d_6), δ: 1.83 (s, 3H, CH_3), 3.88 (s, 2H, CH_2), 7.30—7.82 (m, 8H, H_{arom}), 10.40 (s, 1H, $N{-}H_{benzamide}$), 10.68 (s, 1H, $N{-}H_{quinolone}$), 11.51 (s, 1H, $O{-}H_{quinolinol}$), 13.55 (s, 1H, $O{-}H_{carboxylic}$).

4-Hydroxy-8-methyl-3-(6-oxo-2-phenyl[1,3,4]-oxadiazin-5-yl)methyl-1*H*-quinolin-2-one (*XII*)

To warm (70—80 °C) concentrated sulfuric acid (20 cm^3), finely powdered compound *XI* (5 mmol) was added portion-wise under continuous stirring over 0.5 h, and then stirring was continued for further 0.5 h at room temperature. Afterwards, the reaction mixture was poured onto crushed ice to give a sandy-yellow solid precipitate that was filtered off and crystallized. IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$: 1070, 1110 ν(C—O—C), 1256, 1285, 1460, 1598, 1610—1621 ν(C=N), 1642 $\nu(C{=}O_{quinolone})$, 1743 $\nu(C{=}O_{oxadiazinone})$, 3080—3120 ν(N—H and O—H). ^{1}H NMR spectrum (DMSO-d_6), δ: 1.86 (s, 3H, CH_3), 4.34 (s, 2H, CH_2), 7.34—8.05 (m, 8H, H_{arom}), 10.34 (s, 1H, $N{-}H_{quinolone}$), 11.48 (s, 1H, O—H).

3-(4,5-Dihydro-5-oxo-3-phenyl[1,2,4]triazin-6-yl)methyl-4-hydroxy-8-methyl-1*H*-quinolin-2-one (*XIII*)

A mixture of either *XI* or *XII* (2 mmol) and ammonium acetate (6 mmol) in glacial acetic acid (25 cm^3) was refluxed for 4 h. Then, the reaction mixture was left to stand at room temperature overnight. The obtained yellow crystalline product was filtered off and recrystallized. IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$: 1373, 1478, 1565, 1593, 1600 ν(C=C), 1611—1620 ν(C=N), 1649 $\nu(C{=}O_{quinolone})$, 1672 $\nu(C{=}O_{triazinone})$, 2660—3190 ν(N—H and O—H). ^{1}H NMR spectrum (DMSO-d_6), δ: 1.82 (s, 3H, CH_3), 3.83 (s, 2H, CH_2), 7.20—7.86 (m, 8H, H_{arom}), 10.60 (s, 1H, $N{-}H_{quinolone}$), 10.88 (s, 1H, $N{-}H_{triazinone}$), 11.70 (s, 1H, O—H).

3-(1,2-Dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)pyruvic Acid 2-Hydrazone (*XIV*)

Either compound *V* or *VIII* (5 mmol) was added to hydrazine hydrate (7 mmol, w = 100 %) in ethanol (25 cm^3) and refluxed for 4 h. Then, the reaction mixture was neutralized with dilute acetic acid to give a precipitate, which was filtered off, washed with water, and crystallized. IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$: 1388, 1446, 1482, 1541, 1570, 1585, 1610 ν(C=N), 1646 $\nu(C{=}O_{quinolone})$, 1730 $\nu(C{=}O_{carboxylic})$, 2620—3190 ν(N—H and O—H), 3340—3438 $\nu(NH_2)$. ^{1}H NMR spectrum (DMSO-d_6), δ: 1.81 (s, 3H, CH_3), 3.88 (s, 2H, CH_2), 7.23—7.87 (m, 3H, H_{arom}), 8.18 (s, 2H, NH_2), 10.63 (s, 1H, $N{-}H_{quinolone}$), 11.65 (s, 1H, $O{-}H_{quinolinol}$), 13.25 (s, 1H, $O{-}H_{carboxylic}$).

3-(1,2-Dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)pyruvic Acid 2-Thiosemicarbazone (*XV*) and 4-Phenylthiosemicarbazone (*XVI*)

a) A mixture of either compound *V* or *VIII* (2 mmol), thiosemicarbazide or 4-phenylthiosemicarbazide (2 mmol), and ethanol (50 cm^3, w = 95 %) was refluxed for 4 h. Then, the yellowish-brown deposit that formed during the course of the reaction was filtered off and crystallized to give *XV* and *XVI*, respectively. IR spectrum (KBr), $\tilde{\nu}$(*XV*)/cm^{-1}: 1029, 1084, 1174, 1200, 1260 ν(HNC=S), 1304, 1482, 1544, 1596, 1608 ν(C=N), 1651 ν(C=$O_{quinolone}$), 1729 ν(C=$O_{carboxylic}$), 2620—3190 ν(N—H and O—H), 3355 ν(NH_2); $\tilde{\nu}$(*XVI*)/cm^{-1}: 1075, 1150, 1205, 1273 ν(HNC=S), 1312, 1400, 1489, 1563, 1570, 1605—1610 ν(C=N), 1633, 1647 ν(C=$O_{quinolone}$), 1725 ν(C=$O_{carboxylic}$), 2600—3220 ν(N—H and O—H). ^{1}H NMR spectrum (DMSO-d_6), δ(*XV*): 1.83 (s, 3H, CH_3), 3.86 (s, 2H, CH_2), 7.30—7.68 (m, 3H, H_{arom}), 9.05 (s, 2H, NH_2), 10.20 (s, 1H, N-2—$H_{thiosemicarbazone}$), 10.63 (s, 1H, N—$H_{quinolone}$), 11.53 (s, 1H, O—$H_{quinolinol}$), 13.85 (s, 1H, O—$H_{carboxylic}$); δ(*XVI*): 1.81 (s, 3H, CH_3), 3.88 (s, 2H, CH_2), 7.30—8.05 (m, 8H, H_{arom}), 10.15 (s, 1H, N-4—$H_{thiosemicarbazone}$), 10.25 (s, 1H, N-2—$H_{thiosemicarbazone}$), 10.63 (s, 1H, N—$H_{quinolone}$), 11.53 (s, 1H, O—$H_{quinolinol}$), 13.25 (s, 1H, O—$H_{carboxylic}$).

b) Compound *XIV* (1 mmol) was treated with phenyl isothiocyanate (1.2 mmol) in boiling absolute ethanol (10 cm^3) for 2 h. The reaction mixture was then cooled, and the obtained solid was filtered off, washed with methanol (3 × 5 cm^3) and crystallized to furnish *XVI*, identified by its melting point, mixed melting point, and spectral data.

4-Hydroxy-8-methyl-3-(5-oxo-3-thioxo-2,3,4,5-tetrahydro(or 4-phenyl)[1,2,4]triazin-6-yl)-methyl-1*H*-quinolin-2-ones *XVII* and *XVIII*

a) Either compound *XV* or *XVI* (2 mmol) was treated with sodium ethoxide (4 mmol) in absolute ethanol (25 cm^3) and heated under reflux for 4 h. The reaction mixture was then cooled, diluted with water (50 cm^3) and acidified with hydrochloric acid (5 cm^3, 6.0 M-HCl). The obtained solid, after digestion on a hot water bath, was filtered off and crystallized to give *XVII* or *XVIII*, respectively. IR spectrum (KBr), $\tilde{\nu}$(*XVII*)/cm^{-1}: 1027, 1120, 1240 ν(HNC=S), 1312, 1393, 1450, 1491, 1572, 1610 ν(C=N), 1645 ν(C=$O_{quinolone}$), 1688 ν(C=$O_{triazinone}$), 2864—3167 ν(N—H and O—H); $\tilde{\nu}$(*XVIII*)/cm^{-1}: 1177, 1250 ν(HNC=S), 1327, 1432, 1540, 1590, 1620 ν(C=N), 1643 ν(C=$O_{quinolone}$), 1690 ν(C=$O_{triazinone}$), 2836—3120 ν(N—H and O—H). ^{1}H NMR spectrum (DMSO-d_6), δ(*XVII*): 1.81 (s, 3H, CH_3), 3.82 (s, 2H, CH_2), 7.23—7.82 (m, 3H, H_{arom}), 10.25 (s, 1H, N-2—$H_{triazinone}$), 10.43 (s, 1H, N-4—$H_{triazinone}$), 10.67 (s, 1H, N—$H_{quinolone}$), 11.72 (s, 1H, O—H); δ(*XVIII*): 1.82 (s, 3H, CH_3), 3.68 (s, 2H, CH_2), 7.30—8.05 (m, 8H, H_{arom}), 10.26 (s, 1H, N—$H_{triazinone}$), 10.70 (s, 1H, N—$H_{quinolone}$), 11.65 (s, 1H, O—H).

b) The compound *XIV* (1 mmol) and phenyl isothiocyanate (1.2 mmol) in absolute ethanol (10 cm^3) were refluxed for 2 h. Then the reaction mixture was treated with sodium ethoxide (3 mmol) for further 4 h. The reaction mixture was then cooled, diluted with water (30 cm^3), and acidified with hydrochloric acid (3 cm^3, 6.0 M-HCl). The obtained solid, after digestion on a hot water bath, was filtered off and crystallized to give *XVIII*, identified by its melting point, mixed melting point, and spectral data.

General Procedure for Reaction of Compounds *V* and/or *VIII* with α-Hydrazono-*N*-heterocycles

1-Hydrazono-4-phenylphthalazine (*XIX*), 3-hydrazono[1,2,4]triazino[5,6-*b*]indole (*XXI*), or 2,3-bishydrazonoquinoxaline (*XXIII*), respectively (2 mmol) and either compound *V* or *VIII* (2 mmol) in boiling DMF (20 cm^3) were heated under reflux for 6 h. The solid obtained was collected by filtration, washed with ethanol (3 × 10 cm^3) and crystallized to give compounds *XX*, *XXII* or *XXIV*, respectively.

3-(1,2-Dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)methyl-4-oxo-7-phenyl[1,2,4]triazino[3,4-*a*]phthalazine (*XX*)

IR spectrum (KBr), $\tilde{\nu}$/cm^{-1}: 1051, 1212, 1332, 1430, 1498, 1562, 1602—1615 ν(C=N), 1643 ν(C=$O_{quinolone}$), 1687 ν(C=$O_{triazinone}$), 2880, 3069—3165 ν(N—H and O—H). ^{1}H NMR spectrum (DMSO-d_6), δ: 1.82 (s, 3H, CH_3), 3.55 (s, 2H, CH_2), 7.25—8.10 (m, 12H, H_{arom}), 10.48 (s, 1H, N—$H_{quinolone}$), 11.86 (s, 1H, O—H). Mass spectrum, m/z (I_r/%): 462 (4, $[M + 1]^+$), 461 (16, $[M^+]$), 443 (5, $[M - H_2O]^+$), 433 (46, $[M - CO]^+$), 405 (9), 358 (31), 273 (50), 218 (4), 203 (17), 191 (61), 188 (91), 187 (100), 175 (89), 160 (10), 159 (16), 147 (36), 133 (26), 105 (20), 93 (94), 65 (19).

3-(1,2-Dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)methyl-4-oxo[1,2,4]triazino-[4′,3′:2,3][1,2,4]triazino[5,6-*b*]indole (*XXII*)

IR spectrum (KBr), $\tilde{\nu}$/cm^{-1}: 1140, 1340, 1387, 1449, 1550, 1600—1618 ν(C=N), 1634, 1655 ν(C=$O_{quinolone}$), 1689 ν(C=$O_{triazinone}$), 2871—3207 ν(N—H and O—H). ^{1}H NMR spectrum (DMSO-d_6), δ: 1.82 (s, 3H, CH_3), 3.83 (s, 2H, CH_2), 7.08—7.78 (m, 7H, H_{arom}), 8.89 (s, 1H, N—$H_{triazinoindole}$), 10.47 (s, 1H, N—$H_{quinolone}$), 11.63 (s, 1H, O—H). Mass spectrum, m/z (I_r/%): 426 (3, $[M + 1]^+$), 425 (13, $[M]^+$), 424

(9), 407 (25, $[M - H_2O]^+$), 397 (62, $[M - CO]^+$), 368 (25), 340 (36), 237 (22), 189 (20), 188 (91), 187 (100), 179 (14), 175 (23), 160 (14), 159 (19), 143 (16), 133 (40), 105 (93), 93 (72), 90 (23), 65 (30).

2,7-Bis((1,2-dihydro-4-hydroxy-8-methyl-2-oxoquinolin-3-yl)methyl)-1,8-dioxobis[1,2,4]triazino[4,3-*a*;3′,4′-*c*]quinoxaline (*XXIV*)

IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$: 1107, 1247, 1290, 1345, 1445, 1507, 1540, 1605—1620 ν(C=N), 1633, 1662 ν(C=$O_{quinolone}$), 1690 ν(C=$O_{triazinone}$), 2625—3180 ν(N—H and O—H). ^{1}H NMR spectrum (DMSO-d_6), δ: 1.81 (s, 6H, 2 × CH_3), 3.85 (s, 4H, 2 × CH_2), 7.05—7.85 (m, 10H, H_{arom}), 10.40 (s, 2H, 2 × N—$H_{quinolone}$), 11.68 (s, 2H, 2 × O—H). Mass spectrum, m/z (I_r/%): 642 (1, $[M + 2]^+$), 641 (6, $[M + 1]^+$), 640 (16, $[M]^+$), 638 (18), 622 (13), 612 (51), 610 (73), 604 (40), 584 (23), 556 (17), 530 (17), 528 (16), 466 (13), 438 (37), 412 (26), 266 (17), 238 (28), 210 (9), 189 (18), 188 (81), 187 (95), 179 (81), 175 (100), 174 (65), 160 (15), 133 (60), 105 (85), 93 (25), 90 (15), 65 (36).

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