Synthesis and Cyclization Reactions with Quinolinyl Keto Esters I. Chemical Reactivity of Quinolinyl β-Keto Ester and Quinolinyl α,β-Unsaturated Ketones

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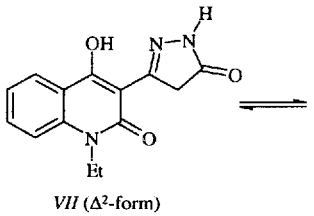
3-Acetyl-1-ethyl-4-hydroxyquinolin-2(1*H*)-one and 1-ethyl-4-hydroxyquinolin-2(1*H*)-one were prepared and subjected to several and different chemical transformations to give novel heterocyclically 3-substituted quinolinone derivatives of expected important biological activity. So the latter compounds were used to obtain β-keto ester and α,β-unsaturated carbonylquinolinones which were used as alternate precursors to produce many new five-membered heterocycles as pyrazolyl, isoxazolyl as substituents to the quinolinone moiety. All the structures of the new products were identified on the basis of their chemical behaviour, elemental and spectral analyses.

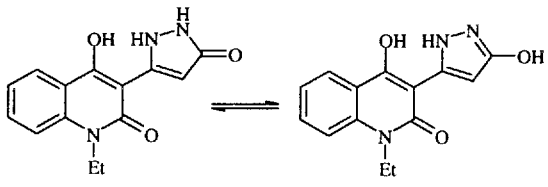
The biological importance of quinolinones [1—4] prompted us to carry out intensive research work for the synthesis of many members of this class of compounds. Within the framework of research related to the chemistry of substituted quinolinones [5—9], we report herein the synthesis and chemistry of some quinolinones substituted at position 3.

Ethyl 3-(1-ethyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-3-oxopropanoate (*V*) and 3-(prop-2-enoyl)-1-ethyl-4-hydroxyquinolin-2(1*H*)-ones *VIa*, *VIb* were synthesized and used as synthons for some novel heterocyclic moieties as substituents to quinolinone, which may have promising biological activity (Scheme 1). The structure of the β-keto ester *V* was established on the basis of its correct C, H, N elemental analysis, IR, ^{1}H NMR, and mass spectral data. IR spectrum indicated the presence of the carbonyl group of ester (C=O$_{ester}$) absorption band at 1724 cm^{-1} and band at 1645 cm^{-1} specific for (C=O) at side chain. ^{1}H NMR spectrum showed signals at δ = 1.21 and 4.21 specific to (OCH_2CH_3) group. The mass spectrum of compound *V* showed molecular ion peak at m/z (I_r/%): 303 (38) and the base peak at m/z = 229 stands for $[C_{13}H_{11}NO_3]^+$ (Chart 1). On the other hand, IR spectrum of compound *VI* showed absorption band at $\tilde{\nu}$/cm^{-1} 1675 specific for (C=O$_{acryloyl}$) group and its ^{1}H NMR spectrum showed signal at δ = 6.99 and 8.25 specific for two olefinic proton groups of the unsaturated system, also *J*, *J* coupling constant (16 Hz) confirmed that the structure assumed *trans* configuration.

Reaction of the β-keto ester *V* with hydrazine hydrate in ethanol gave 3-pyrazolylquinolinone *VII* which was also obtained by hydrazinolysis of the pyrone derivative *I* [10] (Scheme 2). IR (KBr) spectrum of compound *VII* indicated that the pyrazoline ring system is present in the form of Δ^3-pyrazolinone and not Δ^2-pyrazolinone in the solid state. Also, ^{1}H NMR spectrum emphasized that Δ^3-pyrazolinone is the predominate tautomer [11].



VII (Δ^2-form)



VII (Δ^3-form)

Besides all the above spectral and chemical evidences for the structure of compound *VII*, this structure was further confirmed by chemical reactions. Thus, treatment of *VII* with some aromatic amines

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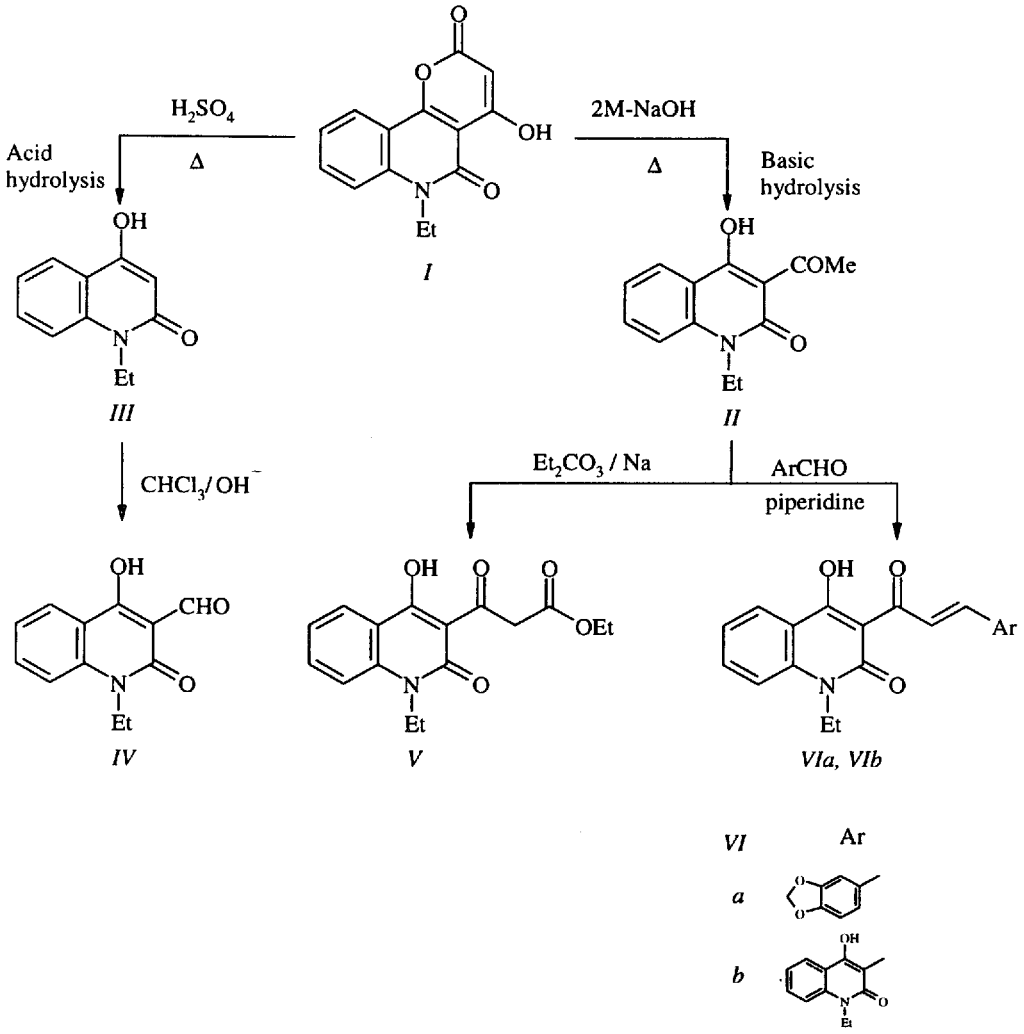


Scheme 1

(namely: 2-aminopyrimidine or 4-aminoantipyrine) and triethyl orthoformate furnished 1-ethyl-4-hydroxy-3-{5-oxo-4-[(pyrimidin-2-yl) (or (antipyrin-4-yl)) aminomethylene]-4,5-dihydro-1*H*-pyrazol-3-yl}quinolin-2(1*H*)-ones (*VIIIa, VIIIb*).

The reactivity of the methylene group of the pyrazolinone *VII* towards coupling with diazonium salts was investigated. Thus, the reaction of compound *VII* with *p*-toluene diazonium chloride or antipyrine-4-diazonium chloride led to interesting hydrazono derivatives *IXa, IXb*. Similarly, condensation reaction of the pyrazolinone *VII* with piperonal or 3-formylquinolinone *IV* in glacial acetic acid and fused sodium acetate afforded the corresponding α,β-unsaturated carbonyl quinolinones *Xa, Xb*.

The reaction of phenylhydrazine and hydroxylammonium chloride with the β-keto ester *V* was also studied. Thus, treatment of compound *V* with phenylhydrazine furnished the pyrazolinone *XI*, while with hydroxylammonium chloride gave isoxazolinone *XII* (Scheme 3). Elemental analysis and spectral data of compounds *XI* and *XII* are in good accordance with the suggested formula. IR spectrum of compound *XI* showed the disappearance of the vibrational bands corresponding to the ester group and the presence of absorption band at 1680 cm^{-1} specific to C=O pyrazolinone.

The reactivity of the methylene group in both pyrazolinone *XI* and isoxazolinone *XII* towards condensation reactions was investigated. Thus, the reaction of compound *XI* with piperonal and 1-ethyl-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxaldehyde (*IV*) furnished the condensation products *XIIIa, XIIIb*. Similarly, treatment of the isoxazolinone *XII* with the same aldehydes gave the corresponding α,β-unsaturated carbonyl compounds *XIVa, XIVb*.

It is of interest to study the competition between the reactivity of α,β-unsaturated ketone moiety and β-keto ester moiety (when present in one molecule) towards reaction with hydrazines. Thus, to prepare derivatives having both moieties, condensation of β-keto ester *V* with both piperonal and/or the aldehyde *IV* was carried out. The products were identified as 3-(benzo[1,3]dioxolan-5-yl) or (1-ethyl-4-hydroxy-2-

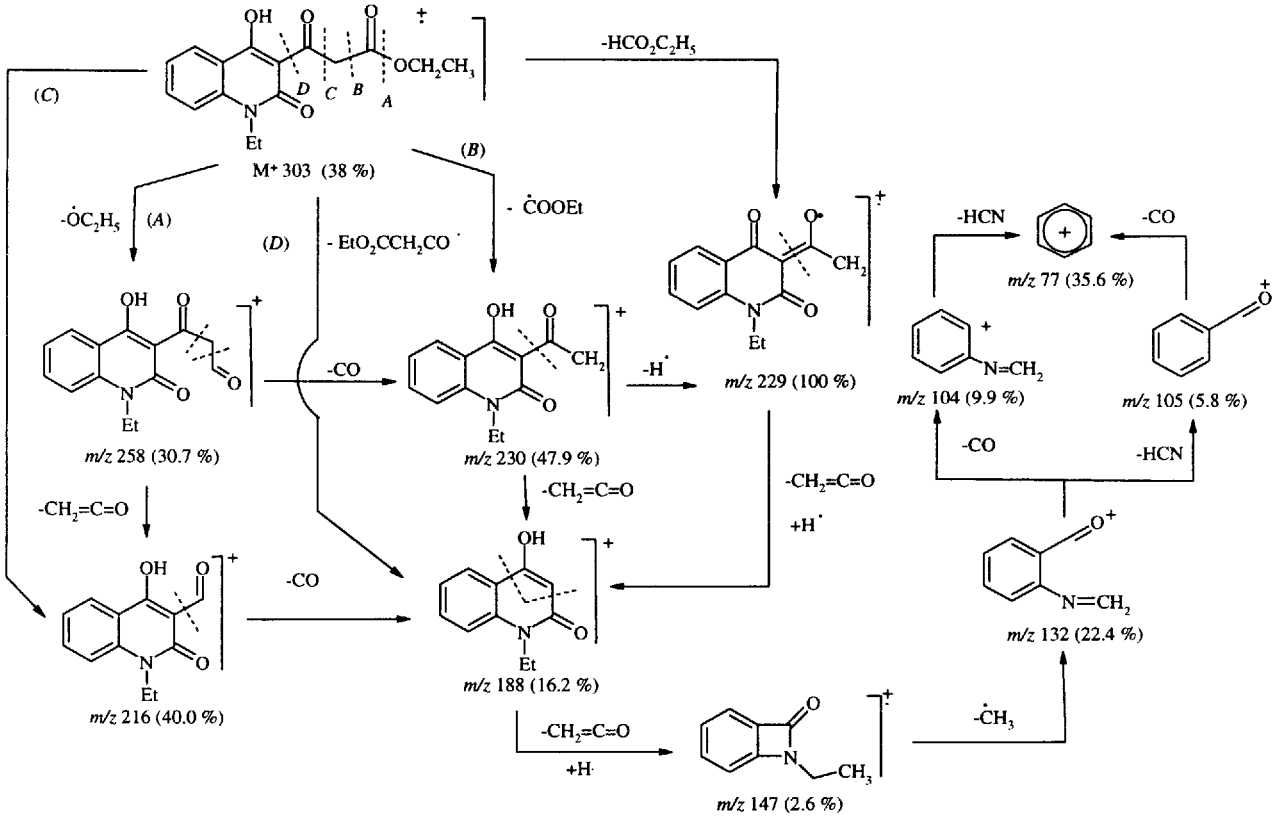
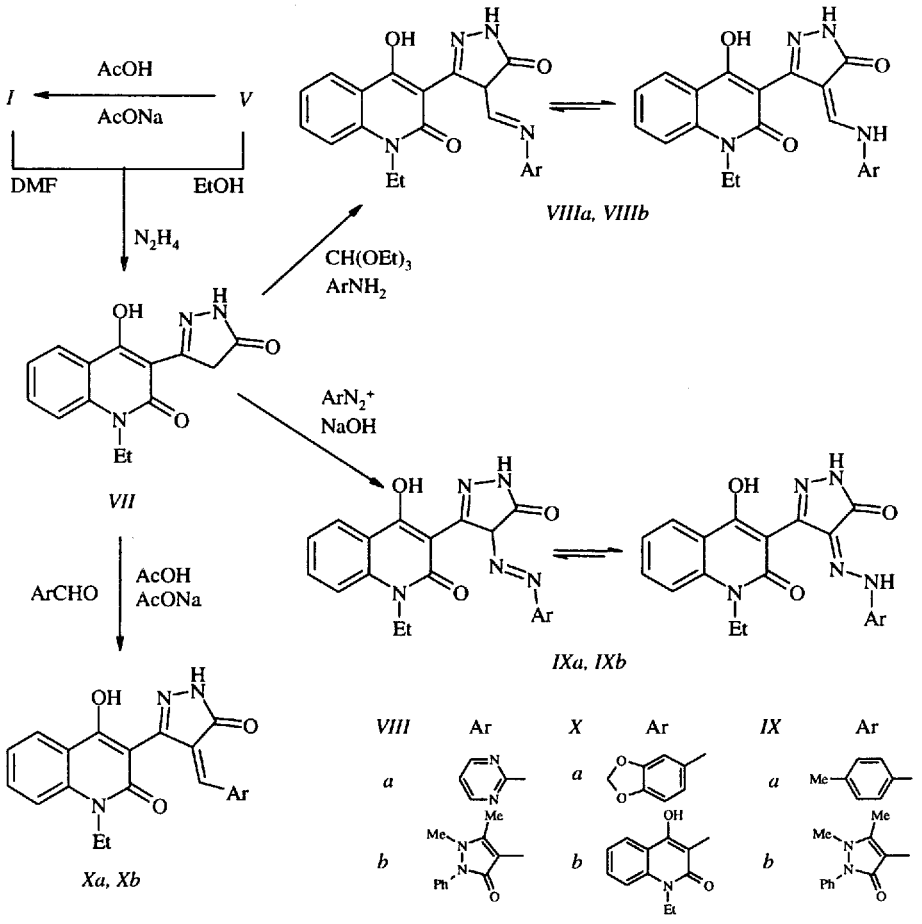
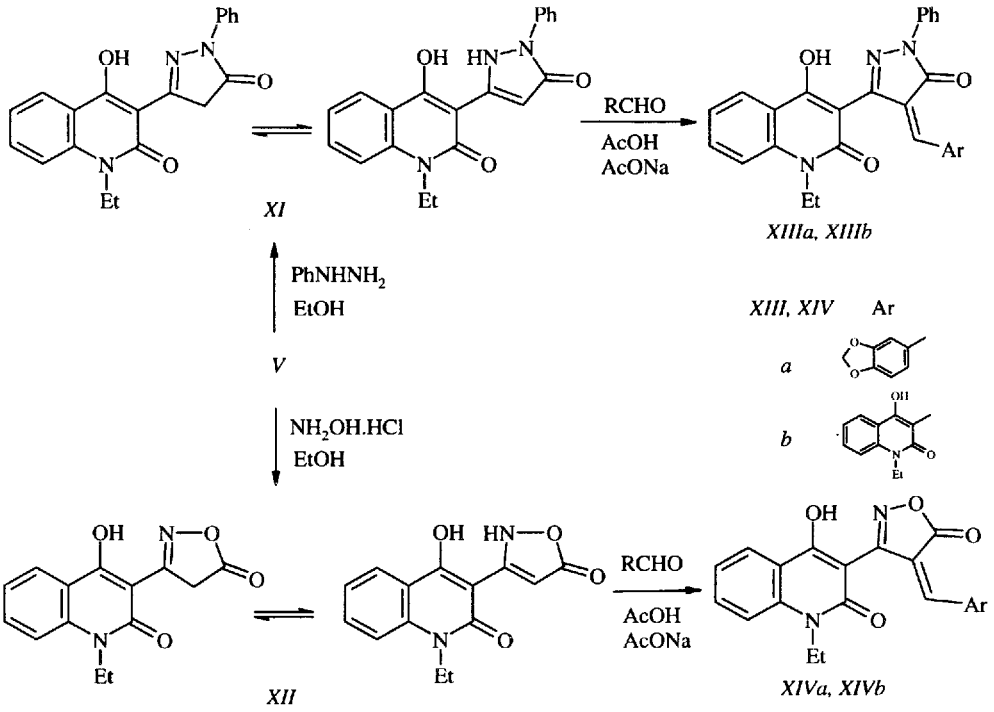


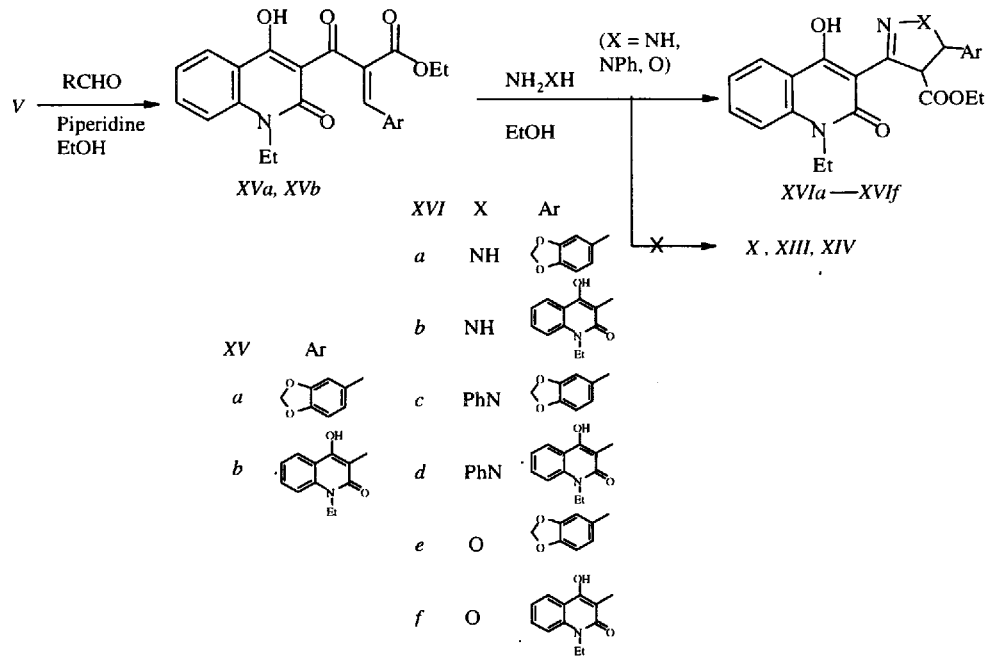
Chart 1. Mass fragmentation pattern of compound *V*



Scheme 2



Scheme 3

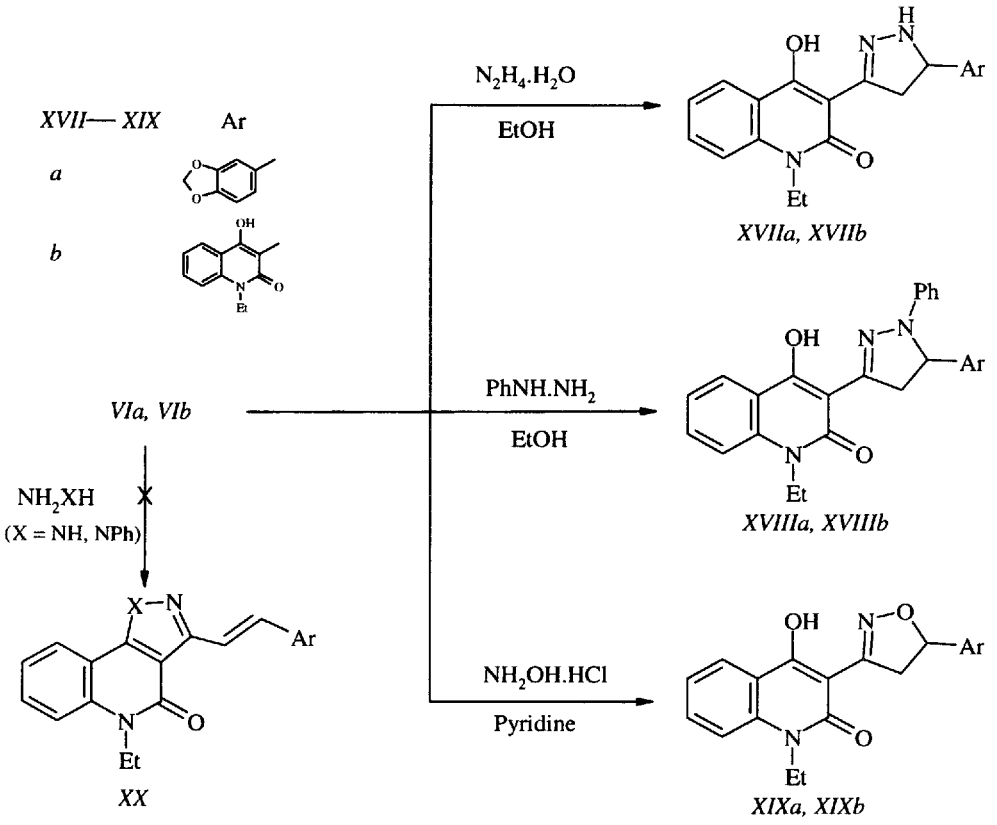


Scheme 4

oxo-1,2-dihydroquinolin-3-yl)acrylic acid ethyl esters (*XVa, XVb*) (Scheme 4). IR spectrum of compound *XV* revealed the presence of absorption bands at 1673 cm^{-1} and 1720 cm^{-1} due to $C{=}O_{\beta\text{-keto}}$ and $C{=}O_{ester}$ groups.

Surprisingly, when the multiactive-centre compounds *XVa, XVb* were allowed to react with hydrazine, phenylhydrazine and/or hydroxylammonium chloride in absolute ethanol, cyclocondensation products were obtained in good yields. The products were identified as *XVIa—XVIf* and the probability of formation of compounds *X, XIII,* and *XIV* was completely excluded by comparing them with previously obtained materials.

The structures of compounds *XVIa—XVIf* were inferred from their correct elemental analyses, IR and ^1H NMR spectra. The IR spectra of the latter compounds supported the proposed structures, where an



Scheme 5

absorption band specific for the ester group appeared at $\tilde{\nu}/cm^{-1}$ from 1727 to 1738. ^1H NMR spectra of *XVIa—XVIf* were found in good accordance with the suggested structures showing specific signals due to OCH_2CH_3 ester.

The formation of *XVIa—XVIf* indicated without any doubt that α,β-unsaturated ketone system is more reactive than β-keto ester one, *i.e.* completion of the reaction is effected by an intramolecular addition-cyclization involving vinyl group (*Michael* addition) and not by condensation involving the carboxylate group, where either nitrogen or oxygen of the preliminarily formed hydrazone or oxime attacks the carbon—carbon double bond and not the ester group.

Taking into consideration the biological activity of both quinolinones and pyrazolines or isoxazolines [12], it was attempted another time to combine both ring skeletons in one molecular frame to produce new compounds of expected biological applications. Thus, the 3-acryloyl derivatives *VIa*, *VIb* were allowed to react with hydrazine hydrate and phenylhydrazine in ethanol and/or hydroxylammonium chloride in pyridine where cyclocondensation products were obtained and identified as pyrazolines *XVIIa*, *XVIIb*, 1-phenylpyrazolines *XVIIIa*, *XVIIIb*, and isoxazolines *XIXa*, *XIXb* (Scheme 5).

The IR and ^1H NMR spectral data and elemental microanalyses of the compounds *XVII—XIX* showed that the cyclization is directed away from the OH group at position 4 of the quinolinone. This was also confirmed by ferric chloride test. ^1H NMR and IR spectra confirmed the structure proposed for the Δ^2-pyrazoline ring system and rejected the probability of the formation of the diazolo[4,5-*c*]quinolinones (*XX*).

EXPERIMENTAL

Melting points are uncorrected and measured in open capillary tubes using a Gallenkamp digital melting point apparatus. IR spectra were recorded on Perkin—Elmer 598 and FT-IR 1650 spectrophotometers, using samples in KBr disks. ^1H NMR spectra were taken on an EM-NMR spectrometer (300 MHz) using DMSO-d_6 as solvent and TMS as internal standard. Mass spectra were obtained on an HP MS-5988 by direct inlet (E = 70 eV). Elemental microanalyses were performed at the Cairo University, Microanalytical Centre. Compounds *I—III* and *IV* were prepared according to the methods cited in literature [13, 14]. Analytical and spectral data are listed in Tables 1 and 2.

Ethyl 3-(1-Ethyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-3-oxopropanoate (*V*)

A mixture of *II* (0.03 mol), finely divided sodium metal (0.15 mol), and dry diethyl carbonate was refluxed for 4 h. The reaction mixture was kept at

Table 1. Analytical Data of the New Compounds

Compound	Formula	w_i(calc.)/% w_i(found)/%			Yield	M.p.	Solvent
	M_r	C	H	N	%	°C	
V	$C_{16}H_{17}NO_5$	63.36	5.65	4.62	65	112—113	EtOH
	303.31	63.90	5.20	4.70			
VIa	$C_{21}H_{17}NO_5$	69.41	4.72	3.85	93	210—212	EtOH/DMF
	363.36	69.30	4.80	4.00			
VIb	$C_{25}H_{22}N_2O_5$	69.76	5.15	6.51	81	240—241	Benzene
	430.45	69.10	5.50	6.60			
VII	$C_{14}H_{13}N_3O_3$	61.99	4.83	15.49	75[a] 69[b]	285—286	EtOH
	271.27	63.20	4.90	15.50			
VIIIa	$C_{19}H_{16}N_6O_3$	60.63	4.28	22.33	77	160—162	EtOH
	376.37	60.40	5.00	22.20			
VIIIb	$C_{26}H_{24}N_6O_4$	64.45	4.99	17.35	79	> 300	EtOH
	484.51	64.21	4.70	17.20			
IXa	$C_{21}H_{19}N_5O_3$	64.77	4.92	17.98	63	240—242	EtOH/DMF
	389.41	63.90	4.70	18.00			
IXb	$C_{25}H_{23}N_7O_4$	61.85	4.78	20.20	62	258—259	DMF/H_2O
	485.49	61.50	4.60	20.00			
Xa	$C_{22}H_{17}N_3O_5$	65.50	4.25	10.42	85	225—227	EtOH/DMF
	403.39	65.60	4.20	10.30			
Xb	$C_{26}H_{22}N_4O_5$	66.37	4.71	11.91	82	> 300	AcOH/H_2O
	470.48	66.70	4.30	11.80			
XI	$C_{20}H_{17}N_3O_3$	69.15	4.93	12.10	84	250—253	EtOH/DMF
	347.37	69.20	4.90	12.00			
XII	$C_{14}H_{12}N_2O_4$	61.76	4.44	10.29	63	188—189	EtOH
	272.26	61.70	4.20	10.40			
XIIIa	$C_{28}H_{21}N_3O_5$	70.14	4.41	8.76	67	275—276	AcOH/H_2O
	479.48	70.30	4.50	9.00			
XIIIb	$C_{32}H_{26}N_4O_5$	70.32	4.79	10.25	58	260—262	Benzene
	546.57	71.20	5.00	10.30			
XIVa	$C_{22}H_{16}N_2O_6$	65.34	3.99	6.93	50	240—241	AcOH
	404.37	65.30	3.90	7.00			
XIVb	$C_{26}H_{21}N_3O_6$	66.24	4.49	8.91	44	280—282	Benzene
	471.46	66.60	4.70	9.00			
XVa	$C_{24}H_{21}NO_7$	66.20	4.86	3.22	92	210—212	Benzene
	435.43	66.20	4.50	3.30			
XVb	$C_{28}H_{26}N_2O_7$	66.92	5.22	5.57	87	220—223	EtOH/DMF
	502.52	66.70	5.20	5.60			
XVIa	$C_{24}H_{23}N_3O_6$	64.14	5.12	9.35	78	140—142	MeOH
	449	64.30	4.90	9.30			
XVIb	$C_{28}H_{28}N_4O_6$	65.11	5.46	10.85	72	182—184	EtOH
	516.55	65.00	5.40	10.90			
XVIc	$C_{30}H_{27}N_3O_6$	68.56	5.18	8.00	75	130—133	MeOH
	525.55	67.99	5.40	8.10			
XVId	$C_{34}H_{32}N_4O_6$	68.91	5.44	9.45	68	160—162	EtOH
	592.64	68.60	5.40	9.50			
XVIe	$C_{24}H_{22}N_2O_7$	63.99	4.92	6.22	48	120—122	MeOH
	450.44	63.60	4.40	6.20			
XVIf	$C_{28}H_{27}N_3O_7$	64.98	5.26	8.12	60	140—143	MeOH
	517.53	64.50	5.10	8.00			
XVIIa	$C_{21}H_{19}N_3O_4$	66.83	5.07	11.13	76	244—245	MeOH
	377.39	66.80	4.20	11.00			
XVIIb	$C_{25}H_{24}N_4O_4$	67.55	5.44	12.60	63	290—292	EtOH/DMF
	444.48	67.80	5.50	12.80			
XVIIIa	$C_{27}H_{23}N_3O_4$	71.51	5.11	9.27	63	235—237	EtOH/DMF
	453.49	71.00	4.90	9.50			
XVIIIb	$C_{31}H_{28}N_4O_4$	71.52	5.42	10.76	56	287—288	DMF
	520.58	71.00	5.30	11.00			
XIXa	$C_{21}H_{18}N_2O_5$	66.66	4.79	7.40	53	229—231	AcOH
	378.38	66.40	4.00	7.50			
XIXb	$C_{25}H_{23}N_3O_5$	67.41	5.20	9.43	41	283—284	Benzene
	445.47	65.70	4.90	9.50			

a, *b* stand for yields of procedures *A* and *B*, respectively.

Table 2. Spectral Data of the New Compounds

Compound	IR, $\tilde{\nu}$/cm^{-1}	^{1}H NMR, δ
V	1630 ν(C=O$_{quinolone}$), 1645 ν(C=O), 1724 ν(C=O$_{ester}$), ≈ 2500 ν(H-bonded OH), 2985 ν(C—H$_{aliph}$)	1.17 (t, 3H, NCH$_2$CH$_3$), 1.21 (t, 3H, OCH$_2$CH$_3$), 4.10 (s, 2H, COCH$_2$CO), 4.12 (q, 2H, NCH$_2$CH$_3$), 4.21 (q, 2H, OCH$_2$CH$_3$), 7.32—8.10 (m, 4H, H$_{arom}$), 12.6 (bs, 1H, OH)
VIa	1045 ν(C—O—C), 1590—1605 ν(C=N, C=C), 1623 ν(C=O$_{quinolone}$), 1680 ν(C=O$_{acryloyl}$), 2570 ν(H-bonded OH), 2930—2990 ν(C—H$_{aliph}$)	1.23 (t, 3H, NCH$_2$CH$_3$), 4.25 (q, 2H, NCH$_2$CH$_3$), 6.10 (s, 2H, OCH$_2$O), 6.99 (d, *J*, *J* = 16 Hz, 1H, H$_{olefin}$), 7.25—8.10 (m, 7H, H$_{arom}$), 8.25 (d, *J*, *J* = 16 Hz, 1H, H$_{olefin}$)
VIb	1587—1610 ν(C=N, C=C), 1637 ν(C=O$_{quinolone}$), 1675 ν(C=O$_{acryloyl}$), 2973 ν(C—H$_{aliph}$)	
VII	1590—1610 ν(C=N), 1632 ν(C=O$_{quinolone}$), 1650 ν(C=O$_{pyrazolone}$), 2600 ν(H-bonded OH), 3203, 3324 ν(NH)	1.22 (t, 3H, NCH$_2$CH$_3$), 4.32 (q, 2H, NCH$_2$CH$_3$), 6.46 (s, 1H, CH$_{pyrazolinone}$), 7.25—8.08 (m, 4H, H$_{arom}$), 11.20 (bs, 1H, NH), 12.60 (bs, 1H, OH), 14.40 (bs, 1H, OH)
VIIIa	1580—1610 ν(C=N), 1625 ν(C=O$_{quinolone}$), 1660 ν(C=O$_{pyrazolone}$), 2500 ν(H-bonded OH), 2978 ν(C—H$_{aliph}$), 3181—3250 ν(NH)	1.21 (t, 3H, NCH$_2$CH$_3$), 4.28 (q, 2H, NCH$_2$CH$_3$), 6.42 (s, 1H, H$_{olefin}$), 6.87 (s, 1H, NH), 7.18—8.00 (m, 7H, H$_{arom}$), 10.10 (bs, 1H, NH), 13.00 (bs, 1H, OH)
VIIIb	1590—1610 ν(C=N), 1635 ν(C=O$_{quinolone}$), 1658 ν(C=O$_{pyrazolone}$), 2600 ν(H-bonded OH), 2990 ν(C—H$_{aliph}$), 3175—3220 ν(NH)	
IXa	1593 ν(C=N), 1631 ν(C=O$_{quinolone}$), 1677 ν(C=O$_{pyrazolone}$), 2600 ν(H-bonded OH), 2932—2975 ν(C—H$_{aliph}$), 3131—3190 ν(NH)	1.20 (t, 3H, NCH$_2$CH$_3$), 4.18 (q, 2H, NCH$_2$CH$_3$), 6.95 (s, 1H, H$_{hydrazono}$), 7.0—8.1 (m, 8H, H$_{arom}$), 11.0 (bs, 1H, NH), 13.40 (bs, 1H, OH)
IXb	1626 ν(C=O$_{quinolone}$), 1650 ν(C=O$_{pyrazolone}$), 1701 ν(C=O$_{antipyrine}$), 2500 ν(H-bonded OH), 2934—2976 ν(C—H$_{aliph}$), 3170—3250 ν(NH)	
Xa	1104 ν(C—O—C), 1607 ν(C=N), 1629 ν(C=O$_{quinolone}$), 1680 ν(C=O$_{pyrazolone}$), 2564 ν(H-bonded OH), 2931—2972 ν(C—H$_{aliph}$), 3190 ν(NH)	1.23 (t, 3H, NCH$_2$CH$_3$), 4.33 (q, 2H, NCH$_2$CH$_3$), 5.97 (s, 2H, OCH$_2$O), 6.75 (s, 1H, CH$_{olefin}$), 6.8—7.93 (m, 7H, H$_{arom}$), 9.9 (bs, 1H, NH), 11.95 (bs, 1H, OH)
Xb	1590—1620 ν(C=N), 1626 ν(C=O$_{quinolone}$), 1685 ν(C=O$_{pyrazolone}$), 2553 ν(H-bonded OH), 2937—2981 ν(C—H$_{aliph}$), 3307 ν(NH)	
XI	1593 ν(C=N), 1624 ν(C=O$_{quinolone}$), 1665 ν(C=O$_{pyrazolone}$), 2566 ν(H-bonded OH), 3205 ν(NH)	1.24 (t, 3H, NCH$_2$CH$_3$), 4.36 (q, 2H, NCH$_2$CH$_3$), 6.50 (s, 1H, H$_{pyrazolone}$), 7.20—8.10 (m, 9H, H$_{arom}$), 10.20 (bs, 1H, NH), 12.22 (bs, 1H, OH)
XII	1643 ν(C=O$_{quinolinone}$), 1725 ν(C=O$_{isoxazolone}$), ≈ 2555 ν(H-bonded OH), 3170 ν(NH)	1.27 (t, 3H, NCH$_2$CH$_3$), 4.37 (q, 2H, NCH$_2$CH$_3$), 7.32—8.00 (m, 5H, H$_{arom}$, H$_{isoxazoline}$), 12.45 (bs, 1H, NH), 14.00 (bs, 1H, OH)
XIIIa	1595—1610 ν(C=N), 1627 ν(C=O$_{quinolone}$), 1684 ν(C=O$_{pyrazolone}$), 2500 ν(H-bonded OH)	1.35 (t, 3H, NCH$_2$CH$_3$), 4.33 (q, 2H, NCH$_2$CH$_3$), 6.08 (s, 2H, OCH$_2$O), 6.49 (s, 1H, CH$_{olefin}$), 7.23—8.19 (m, 12H, H$_{arom}$), 13.00 (bs, 1H, OH)
XIIIb	1598—1605 ν(C=N), 1627 ν(C=O$_{quinolone}$), 1675 ν(C=O$_{pyrazolone}$), 2500 ν(H-bonded OH), 2931—2973 ν(C—H$_{aliph}$)	
XIVa	1037, 1088 ν(O—C—O), 1590—1606 ν(C=N), 1627 ν(C=O$_{quinolone}$), 1734 ν(C=O$_{isoxazolone}$), 2566 ν(H-bonded OH)	1.21 (t, 3H, NCH$_2$CH$_3$), 4.34 (q, 2H, NCH$_2$CH$_3$), 5.93 (s, 2H, OCH$_2$O), 6.53 (s, 1H, CH$_{olefin}$), 6.73—8.08 (m, 7H, H$_{arom}$), 12.78 (bs, 1H, OH)
XIVb	1600 ν(C=C), 1665, 1650 ν(C=O$_{quinolone}$), 1734 ν(C=O$_{isoxazole}$), 2500 ν(H-bonded OH)	
XVa	1629 ν(C=O$_{quinolone}$), 1673 ν(C=O$_{\beta\text{-keto}}$), 1720 ν(C=O$_{ester}$), 2563 ν(H-bonded OH), 2931—2975 ν(C—H$_{aliph}$)	1.20 (t, 3H, NCH$_2$CH$_3$), 1.25 (t, 3H, OCH$_2$CH$_3$), 4.11 (q, 2H, NCH$_2$CH$_3$), 4.20 (q, 2H, OCH$_2$CH$_3$), 5.95 (s, 2H, OCH$_2$O), 6.44 (s, 1H, H$_{olefin}$), 7.31—8.10 (m, 7H, H$_{arom}$), 12.66 (bs, 1H, OH)

Table 2 (Continued)

Compound	IR, $\tilde{\nu}$/cm^{-1}	^{1}H NMR, δ
XVb	1628 ν(C=O$_{quinolone}$), 1670 ν(C=O$_{\beta\text{-keto}}$), 1737 ν(C=O$_{ester}$), 2562 ν(H-bonded OH), 2931—2973 ν(C—H$_{aliph}$)	
XVIa	1037, 1117 ν(C—O—C), 1625 ν(C=O$_{quinolone}$), 1727 ν(C=O$_{ester}$), ≈ 2565 ν(H-bonded OH), 2923—2971 ν(C—H$_{aliph}$)	1.20 (t, 3H, NCH$_2$CH$_3$), 1.25 (t, 3H, OCH$_2$CH$_3$), 3.65 (d, 1H, C-5—H$_{pyrazoline}$), 4.20 (q, 2H, NCH$_2$CH$_3$), 4.33 (q, 2H, OCH$_2$CH$_3$), 5.95 (s, 2H, OCH$_2$O), 6.67—8.00 (m, 8H, H$_{arom}$ + C-4—H$_{pyrazoline}$), 10.00 (bs, 1H, NH), 13.95 (bs, 1H, OH)
XVIb	1604 ν(C=N), 1626 ν(C=O$_{quinolone}$), 1738 ν(C=O$_{ester}$), ≈ 2500 ν(H-bonded OH), 2929—2971 ν(C—H$_{aliph}$)	
XVIc	1037, 1117 ν(C—O—C), 1607 ν(C=N), 1630 ν(C=O$_{quinolone}$), 1730 ν(C=O$_{ester}$), ≈ 2564 ν(H-bonded OH), 2929—2974 ν(C—H$_{aliph}$)	1.17 (t, 3H, NCH$_2$CH$_3$), 1.26 (t, 3H, OCH$_2$CH$_3$), 3.60 (d, 1H, C-4—H$_{pyrazoline}$), 4.18 (q, 2H, NCH$_2$CH$_3$), 4.35 (q, 2H, OCH$_2$CH$_3$), 5.95 (s, 2H, OCH$_2$O), 6.68—7.92 (m, 13H, H$_{arom}$ + C-5—H$_{pyrazoline}$), 13.80 (bs, 1H, OH)
XVId	1558—1605 ν(C=N, C=C), 1637 ν(C=O$_{quinolone}$), 1730 ν(C=O$_{ester}$), ≈ 2673 ν(H-bonded OH), 2943—2982 ν(C—H$_{aliph}$)	
XVIe	1029, 1132 ν(C—O—C), 1630 ν(C=O$_{quinolone}$), 1735 ν(C=O$_{ester}$), ≈ 2500 ν(H-bonded OH), 2935—2976 ν(C—H$_{aliph}$)	1.21 (t, 3H, NCH$_2$CH$_3$), 1.24 (t, 3H, OCH$_2$CH$_3$), 3.70 (d, 1H, C-4—H$_{isoxazoline}$), 4.22 (q, 2H, NCH$_2$CH$_3$), 4.33 (q, 2H, OCH$_2$CH$_3$), 5.95 (s, 2H, OCH$_2$O), 6.60—8.0 (m, 8H, H$_{arom}$ + C-5—H$_{isoxazoline}$), 13.40 (bs, 1H, OH)
XVIf	1605 ν(C=N), 1627, 1659 ν(C=O$_{quinolone}$), 1742 ν(C=O$_{ester}$), ≈ 2567 ν(H-bonded OH), 2930—2977 ν(C—H$_{aliph}$)	
XVIIb	1630, 1635 ν(C=O$_{quinolone}$), ≈ 2550 ν(H-bonded OH), 3195—3210 ν(NH)	
XVIIIa	1046 ν(C—O—C), 1590—1610 ν(C=N), 1650 ν(C=O), 2700 ν(H-bonded OH)	1.21 (t, 3H, NCH$_2$CH$_3$), 3.48—3.56 (d, 2H, CH$_{2pyrazoline}$), 4.19—4.25 (m, 3H, NCH$_2$CH$_3$ + C-5—H$_{pyrazoline}$), 5.98 (s, 2H, OCH$_2$O), 6.80—8.10 (m, 12H, H$_{arom}$), 13.4 (bs, 1H, OH)
XVIIIb	1595—1605 ν(C=N, C=C), 1650, 1635 ν(C=O$_{quinolone}$), 2600 ν(H-bonded OH), 2995 ν(C—H$_{aliph}$)	
XIXa	1601—1610 ν(C=N), 1660 ν(C=O), 2600 ν(H-bonded OH), 2931—2976 ν(C—H$_{aliph}$)	1.20 (t, 3H, NCH$_2$CH$_3$), 4.18—4.40 (m, 4H, NCH$_2$CH$_3$ + CH$_{2isoxazoline}$), 5.31 (t, 1H, C-5—H$_{isoxazoline}$), 5.98 (s, 2H, OCH$_2$O), 6.90—8.0 (m, 7H, H$_{arom}$), 13.60 (bs, 1H, OH)
XIXb	1640, 1631 ν(C=O$_{quinolone}$), 2990 ν(C—H$_{aliph}$), 3137 ν(NH)	

room temperature overnight, then poured into dilute acetic acid. The precipitate that formed was filtered off, washed with water and crystallized.

3-[(2*E*)-3-(1,3-Benzodioxolan-5-yl)prop-2-enoyl]-1-ethyl-4-hydroxyquinolin-2(1*H*)-one (*VIa*) and 1-Ethyl-3-[(*E*)-3-(1-ethyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-2-propenoyl]-4-hydroxyquinolin-2(1*H*)-one (*VIb*)

A mixture of *II* (0.01 mol), piperonal or the aldehyde *IV* (0.01 mol) and one drop of piperidine was heated on a boiling water bath for 4 h. The reaction mixture was triturated with ethanol and the solid so obtained was filtered off, washed with diethyl ether and crystallized.

1-Ethyl-4-hydroxy-3-(5-oxo-4,5-dihydro-1*H*-pyrazol-3-yl)quinolin-2(1*H*)-one (*VII*)

Method A. A mixture of *V* (0.01 mol) and hydrazine hydrate (0.01 mol) in absolute ethanol (10 cm^3) was refluxed for 4 h. The solid product that separated on cooling was filtered off and crystallized.

Method B. To a solution of compound *I* (0.1 mol) in DMF (20 cm^3), hydrazine hydrate (0.15 mol) was added and the reaction mixture was refluxed for 5 h. The mixture was then poured into ice-cold water con-

taining diluted hydrochloric acid, afterwards the precipitate so formed was filtered off and crystallized.

1-Ethyl-4-hydroxy-3-{5-oxo-4-[(pyrimidin-2-yl)aminomethylene]-4,5-dihydro-1*H*-pyrazol-3-yl}quinolin-2(1*H*)-one (*VIIIa*) and 1-Ethyl-4-hydroxy-3-{5-oxo-4-[(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)aminomethylene]-4,5-dihydro-1*H*-pyrazol-3-yl}quinolin-2(1*H*)-one (*VIIIb*)

A mixture of *VII* (0.01 mol), triethyl orthoformate (0.01 mol), and 2-aminopyrimidine or 4-aminoantipyrine in ethylene glycol (20 cm^3) was heated with stirring at 110—115 °C for 20 min and the temperature was raised gradually to 190 °C during 1 h. Then the reaction mixture was left to cool at room temperature and treated with 50 cm^3 of methanol. The precipitate that formed was collected, washed with methanol and crystallized.

1-Ethyl-4-hydroxy-3-{4-[(*E*)-2-(4-methylphenyl)hydrazono]-5-oxo-4,5-dihydro-1*H*-pyrazol-3-yl}quinolin-2(1*H*)-one (*IXa*) and 3-{4-[(*E*)-2-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)hydrazono]-5-oxo-4,5-dihydro-1*H*-pyrazol-3-yl)quinolin-2(1*H*)-one (*IXb*)

To a stirred solution of amine (0.01 mol) in hydrochloric acid (0.02 mol; 10 cm^3 of water) sodium nitrite (0.01 mol) was added dropwise at 0—5 °C. The resulting solution was then gradually added with stirring to a solution of pyrazolinone *VII* (0.01 mol) in sodium hydroxide (0.01 mol) in ice bath, the product so formed during the stirring was filtered off and crystallized.

3-[4-(1,3-Benzodioxolan-5-ylmethylene)-5-oxo-4,5-dihydro-1*H*-pyrazol-3-yl]-1-ethyl-4-hydroxyquinolin-2(1*H*)-one (*Xa*) and 1-Ethyl-3-{[3-(1-ethyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-5-oxo-1,5-dihydro-4*H*-pyrazol-4-ylidene]methyl}-4-hydroxyquinolin-2(1*H*)-one (*Xb*)

A mixture of pyrazolinone *VII* (0.01 mol) and piperonal or the aldehyde *IV* (0.01 mol) in glacial acetic acid (25 cm^3) and fused sodium acetate (0.02 mol) was refluxed for 4 h. The reaction mixture was left to cool and it was poured into crushed ice. The precipitate so formed was collected by filtration and crystallized.

1-Ethyl-4-hydroxy-3-(5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)quinolin-2(1*H*)-one (*XI*) and 1-Ethyl-4-hydroxy-3-(5-oxo-4,5-dihydroisoxazol-3-yl)quinolin-2(1*H*)-one (*XII*)

A solution of *V* (0.01 mol) with phenylhydrazine or hydroxylammonium chloride (0.01 mol) was refluxed in ethanol (15 cm^3) for 5 h, then the mixture was cooled to the room temperature. The solid so formed was filtered off, dried well and crystallized.

3-{4-[1-(1,3-Benzodioxolan-5-yl)- (*XIIIa*) or (1-Ethyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)methylidene]-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl}-1-ethyl-4-hydroxyquinolin-2(1*H*)-one (*XIIIb*) and 4-[1-(1,3-Benzodioxolan-5-yl)- (*XIVa*) or (1-Ethyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)methylidene]-3-(1-ethyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-4,5-dihydro-5-isoxazolone (*XIVb*)

Using the same method as for preparation of *X*, treatment of compounds *XI, XII* with piperonal or the aldehyde *IV* afforded *XIIIa, XIIIb* and *XIVa, XIVb*.

Ethyl 3-[(1,3-Benzodioxolan-5-yl)- (*XVa*) or (1-Ethyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)]-2-[(1-ethyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)carbonyl]-2-propenoate (*XVb*)

Similarly, using the same method as for preparation of compound *VI*, treatment of compound *V* with piperonal or the aldehyde *IV* yielded the compounds *XVa, XVb*.

Ethyl 5-Ar-3-(1-ethyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-4,5-dihydro-1*H*-4-pyrazolecarboxylates (*XVIa*—*XVId*) and -4,5-dihydro-4-isoxazolecarboxylates (*XVIe, XVIf*)

A solution of the compound *XV* (0.01 mol) in absolute ethanol (50 cm^3) was treated with hydrazine hydrate, phenylhydrazine or hydroxylammonium chloride (0.012 mol). The reaction mixture was refluxed for 3 h, then cooled and the precipitate so formed was filtered off and crystallized.

3-[5-(1,3-Benzodioxolan-5-yl)-4,5-dihydro-1*H*-pyrazol-3-yl]-1-ethyl-4-hydroxyquinolin-2(1*H*)-one (*XVIIa*) and 3,5-Di(1-ethyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-4,5-dihydro-1*H*-pyrazole (*XVIIb*)

To a solution of the compound *VI* (0.01 mol) in ethanol (20 cm^3) hydrazine hydrate (0.01 mol) was added. The reaction mixture was refluxed for 5 h, then cooled and poured into water. The solid that deposited was filtered off and crystallized.

3-[5-(1,3-Benzodioxolan-5-yl)-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]-1-ethyl-4-hydroxy-

quinolin-2(1*H*)-one (*XVIIIa*) and 3,5-Di(1-ethyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-1-phenyl-4,5-dihydro-1*H*-pyrazole (*XVIIIb*)

A procedure similar to that used for obtaining of compound *XVII* was utilized to prepare the phenylpyrazolines (*XVIIIa, XVIIIb*) from the proper derivatives of compound *VI* and phenylhydrazine.

3-[5-(1,3-Benzodioxolan-5-yl)-4,5-dihydroisoxazol-3-yl]-1-ethyl-4-hydroxyquinolin-2(1*H*)-one (*XIXa*) and 3,5-Di(1-ethyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-4,5-dihydroisoxazole (*XIXb*)

A mixture of *VI* (0.01 mol) and hydroxylammonium chloride (0.01 mol) in pyridine (20 cm^3) was heated under reflux for 6 h. The reaction mixture was cooled to room temperature and diluted with cold water (20 cm^3). The solid so obtained on acidification of the reaction mixture was collected by filtration and crystallized.

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