Synthesis of New 3-Acryloyl-1,2-dihydro-4-hydroxy-1-methyl-2-oxoquinoline Derivatives and their Behaviour towards Some Nucleophiles

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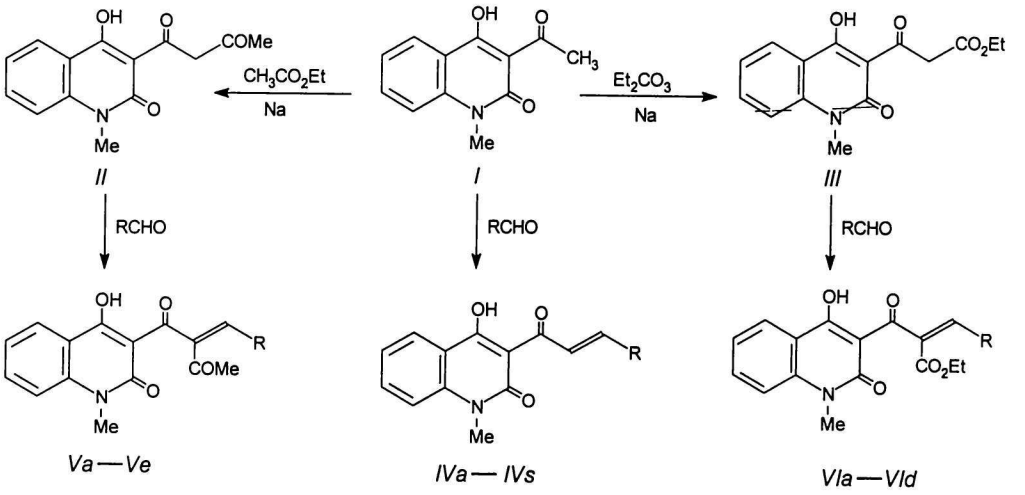
Many new 3-acryloyl-1,2-dihydro-4-hydroxy-1-methyl-2-quinolone derivatives have been synthesized. The addition of a series of aromatic amines and thiols to the activated carbon—carbon double bond of the acryloyl side chain is described. The behaviour of some of these acryloyl derivatives towards 1,2-bifunctional nucleophiles: hydrazine, phenylhydrazine, and hydroxylamine, has been investigated and cyclocondensation reactions were found to take place, affording 3-(3-pyrazolinyl/isoxazolinyl)-2-quinolones. Addition of bromine to the 3-(5-styryl-3-pyrazolinyl/isoxazolinyl)-2-quinolones furnished the corresponding 1,2-dibromophenethyl derivatives which upon cyclization with *o*-phenylenediamine and/or *o*-aminothiophenol afforded novel heterotricyclic isolated systems of expected biological activity.

Due to their associated important biological activities, quinolines have attracted a continuous interest as a class of vital pharmacologically active heterocyclic compounds [1—3]. Currently, the present work is an extension of the developed program on synthesis and reactions of 2-quinolones in our laboratory [4—7].

This paper is focused on the synthesis of some new 3-pyrazolinyl- and 3-isoxazolinyl-2-quinolones. The approach to these ring systems utilized a Claisen—Schmidt reaction of the readily available 3-acetyl-1,2-dihydro-4-hydroxy-1-methyl-2-quinolone (*I*), 3-acetoacetyl-1,2-dihydro-4-hydroxy-1-methyl-2-quinolone (*II*), and 3-ethoxycarbonylacetyl-1,2-dihydro-4-hydroxy-1-methyl-2-quinolone (*III*) [8] with aromatic aldehydes to afford the corresponding 3-acryloyl derivatives *IVa—IVs*, *Va—Ve*, and *VIa—VId*, respectively (Scheme 1, Table 1). Due to the increase of double—single bonds conjugation in compound *IVa* (R = C_6H_5—CH=CH), its UV spectrum showed a strong absorption band at λ_{max}(acetone)/nm = 389.6. Comparison of the maxima of the parent acetyl derivative *I* and the cinnamylidene product *IVa* indicated that an increment of λ_{max} equaled 29 nm, thus confirming the proposed structure of the latter compound.



Scheme 1

Table 1. Characterization of the Compounds *IV*—*VI*

Compound	R	Formula M_r	Yield %	M.p. °C	Solvent
IVa	Styryl	$C_{21}H_{17}NO_3$ 331	86	180[a]	Benzene
IVb	3,4-Methylenedioxyphenyl	$C_{20}H_{15}NO_5$ 349	93	212	Anisole
IVc	4-Dimethylaminophenyl	$C_{21}H_{20}N_2O_3$ 348	75	170	DMF
IVd	2-Chlorophenyl	$C_{19}H_{14}NO_3Cl$ 339.5	96	210	Dioxane
IVe	4-Chlorophenyl	$C_{19}H_{14}NO_3Cl$ 339.5	93	182	Acetic acid
IVf	2,6-Dichlorophenyl	$C_{19}H_{13}NO_3Cl_2$ 374	96	132	Acetic acid
IVg	2-Hydroxyphenyl	$C_{19}H_{15}NO_4$ 321	95	142	Acetic acid
IVh	3-Hydroxyphenyl	$C_{19}H_{15}NO_4$ 321	95	140	Acetic acid
IVi	4-Hydroxyphenyl	$C_{19}H_{15}NO_4$ 321	96	250	Acetic acid
IVj	4-Methylphenyl	$C_{20}H_{17}NO_3$ 319	95	162	Acetic acid
IVk	2,5-Dimethylphenyl	$C_{21}H_{19}NO_3$ 333	89	160	Acetic acid
IVl	2-Nitrophenyl	$C_{19}H_{14}N_2O_5$ 350	78	163	Acetic acid
IVm	4-Nitrophenyl	$C_{19}H_{14}N_2O_5$ 350	86	154	Acetic acid
IVn	2-Methoxyphenyl	$C_{20}H_{17}NO_4$ 335	97	192	Dioxane
IVo	4-Methoxyphenyl	$C_{20}H_{17}NO_4$ 335	84	182[b]	Dioxane
IVp	Phenyl	$C_{19}H_{15}NO_3$ 305	83	170[c]	Acetic acid
IVq	2-Hydroxy-1-naphthyl	$C_{23}H_{17}NO_4$ 371	90	142	Acetic acid
IVr	2-Furyl	$C_{17}H_{13}NO_4$ 295	96	106	Acetic acid
IVs	3-Indolyl	$C_{21}H_{16}N_2O_3$ 344	93	142	Acetic acid
Va	Styryl	$C_{21}H_{19}NO_4$ 373	81	119	Methanol
Vb	3,4-Methylenedioxyphenyl	$C_{22}H_{17}NO_6$ 391	92	192	Acetic acid
Vc	4-Dimethylaminophenyl	$C_{23}H_{22}N_2O_4$ 390	75	177	Ethanol
Vd	2,6-Dichlorophenyl	$C_{21}H_{15}NO_4Cl_2$ 416	67	>280	DMF
Ve	Phenyl	$C_{21}H_{17}NO_4$ 347	88	265	DMF
VIa	Styryl	$C_{24}H_{21}NO_5$ 403	76	125	Acetic acid
VIb	3,4-Methylenedioxyphenyl	$C_{23}H_{19}NO_7$ 421	74	243[d]	Benzene
VIc	4-Dimethylaminophenyl	$C_{24}H_{24}N_2O_5$ 420	68	217[e]	Dioxane
VId	4-Chlorophenyl	$C_{22}H_{18}NO_5Cl$ 411.5	82	136	Benzene

a) Ref. [7], m.p. = 182—183 °C; *b*) Ref. [7], m.p. = 172—173 °C; *c*) Ref. [7], m.p. = 170—172 °C; *d*) Ref. [8], m.p. = 243 °C; *e*) Ref. [8], m.p. = 217 °C.

It is postulated that diverse pharmacological actions of 3-substituted 4-hydroxy-2-quinolones may back to the presence of a basic centre, linked to the quinoline moiety by a long carbonyl side chain [2]. Therefore, the addition reaction of many aromatic amines with the 3-acryloyl or 3-cinnamylideneacetyl derivatives was carried out to obtain more compounds of this category. Treating some of the 3-

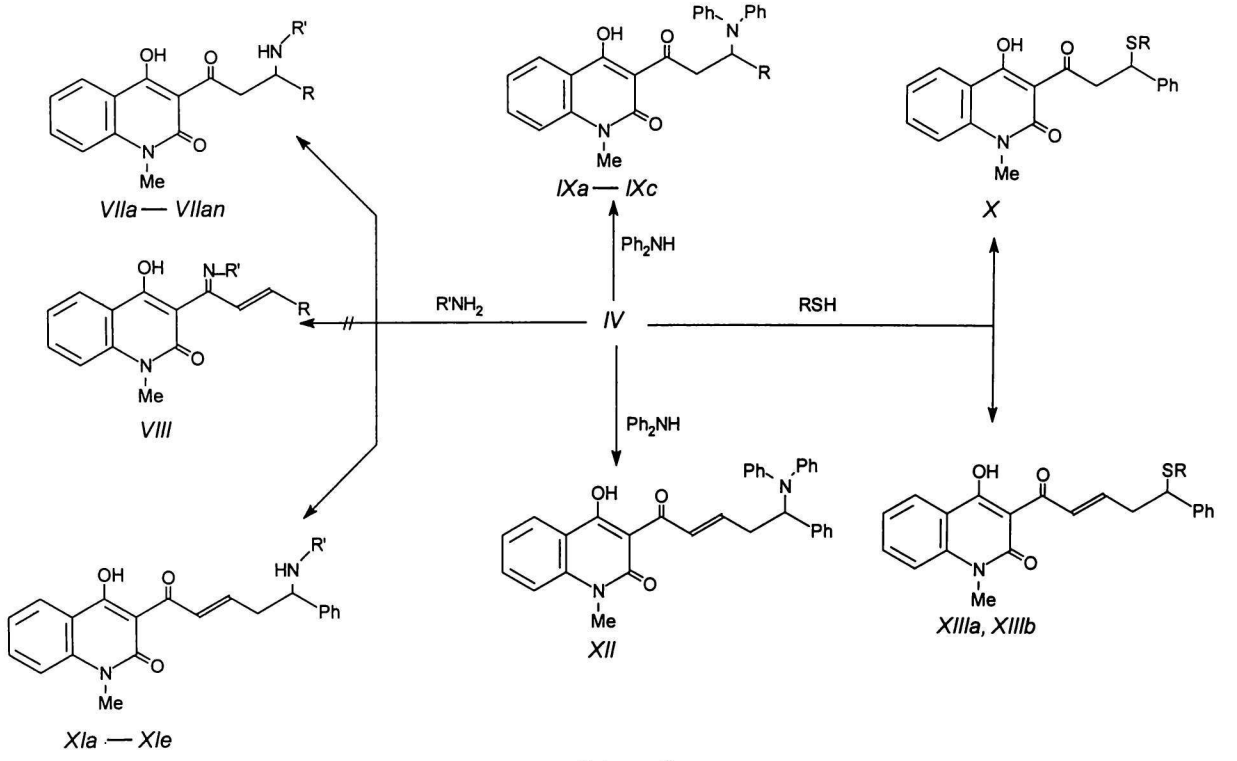
Table 2. Characterization of the Compounds *VIIa*—*VIIan*

Compound	R	R′	Formula M_r	Yield %	M.p.* °C
VIIa	2-Hydroxyphenyl	4-Methoxyphenyl	$C_{26}H_{24}N_2O_5$ 444	76	112
VIIb	3,4-Methylenedioxyphenyl	4-Methoxyphenyl	$C_{27}H_{24}N_2O_6$ 472	70	126
VIIc	4-Dimethylaminophenyl	4-Methoxyphenyl	$C_{28}H_{29}N_3O_4$ 471	85	122
VIId	2-Hydroxy-1-naphthyl	4-Methoxyphenyl	$C_{30}H_{26}N_2O_4$ 478	83	150
VIIe	3,4-Methylenedioxyphenyl	4-Methylphenyl	$C_{27}H_{24}N_2O_5$ 456	73	80
VIIf	4-Dimethylaminophenyl	4-Methylphenyl	$C_{28}H_{29}N_3O_3$ 455	81	168
VIIg	3,4-Methylenedioxyphenyl	4-Nitrophenyl	$C_{26}H_{21}N_3O_7$ 487	77	130
VIIh	4-Dimethylaminophenyl	4-Nitrophenyl	$C_{27}H_{26}N_4O_5$ 486	82	111
VIIi	2-Hydroxy-1-naphthyl	4-Nitrophenyl	$C_{29}H_{23}N_3O_6$ 509	79	140
VIIj	2-Furyl	4-Nitrophenyl	$C_{23}H_{19}N_3O_6$ 433	67	143
VIIk	3,4-Methylenedioxyphenyl	4-Aminophenyl	$C_{26}H_{23}N_3O_5$ 457	81	266
VIIl	4-Dimethylaminophenyl	4-Aminophenyl	$C_{27}H_{28}N_4O_3$ 456	77	162
VIIm	2-Hydroxy-1-naphthyl	4-Aminophenyl	$C_{29}H_{25}N_3O_4$ 479	83	94
VIIn	2-Furyl	4-Aminophenyl	$C_{23}H_{21}N_3O_4$ 403	85	154
VIIo	3,4-Methylenedioxyphenyl	3-Aminophenyl	$C_{26}H_{23}N_3O_5$ 457	74	92
VIIp	4-Dimethylaminophenyl	3-Aminophenyl	$C_{27}H_{28}N_4O_3$ 456	72	142
VIIq	2-Hydroxy-1-naphthyl	3-Aminophenyl	$C_{29}H_{25}N_3O_4$ 479	70	110
VIIr	2-Furyl	3-Aminophenyl	$C_{23}H_{21}N_3O_4$ 403	79	158
VIIs	4-Dimethylaminophenyl	4-Chlorophenyl	$C_{27}H_{26}N_3O_3Cl$ 475.5	88	152
VIIt	3,4-Methylenedioxyphenyl	2-Bromophenyl	$C_{26}H_{21}N_2O_5Br$ 521	73	138
VIIu	4-Dimethylaminophenyl	2-Bromophenyl	$C_{27}H_{26}N_3O_3Br$ 520	58	100
VIIv	3,4-Methylenedioxyphenyl	3-Pyridyl	$C_{25}H_{21}N_3O_5$ 443	60	160
VIIw	4-Dimethylaminophenyl	3-Pyridyl	$C_{26}H_{26}N_4O_3$ 442	79	148
VIIx	2-Hydroxy-1-naphthyl	3-Pyridyl	$C_{28}H_{23}N_3O_4$ 465	78	284
VIIy	2-Furyl	3-Pyridyl	$C_{22}H_{19}N_3O_4$ 389	68	172
VIIz	3,4-Methylenedioxyphenyl	3-Picolyl	$C_{26}H_{23}N_3O_5$ 457	75	118
VIIaa	2-Hydroxy-1-naphthyl	3-Picolyl	$C_{29}H_{25}N_3O_4$ 479	71	130
VIIab	2-Furyl	3-Picolyl	$C_{23}H_{21}N_3O_4$ 403	59	206
VIIac	2-Hydroxyphenyl	8-Amino-1-naphthyl	$C_{29}H_{25}N_3O_4$ 479	80	156
VIIad	3,4-Methylenedioxyphenyl	8-Amino-1-naphthyl	$C_{30}H_{25}N_3O_5$ 507	68	192
VIIae	4-Dimethylaminophenyl	8-Amino-1-naphthyl	$C_{31}H_{30}N_4O_3$ 506	53	136
VIIaf	2-Furyl	8-Amino-1-naphthyl	$C_{27}H_{23}N_3O_4$ 453	67	196

Table 2 (Continued)

Compound	R	R′	Formula M_r	Yield %	M.p.* °C
VIIag	3,4-Methylenedioxyphenyl	1-Naphthyl	$C_{30}H_{24}N_2O_5$ 492	64	182
VIIah	4-Dimethylaminophenyl	1-Naphthyl	$C_{31}H_{29}N_3O_3$ 491	58	150
VIIai	2-Hydroxy-1-naphthyl	1-Naphthyl	$C_{33}H_{26}N_2O_4$ 514	59	102
VIIaj	4-Dimethylaminophenyl	2-Naphthyl	$C_{31}H_{29}N_3O_3$ 491	72	192
VIIak	2-Furyl	2-Naphthyl	$C_{27}H_{22}N_2O_4$ 438	60	176
VIIal	4-Chlorophenyl	2-Naphthyl	$C_{29}H_{23}N_2O_3Cl$ 482.5	65	92
VIIam	4-Dimethylaminophenyl	4-Antipyrinyl	$C_{32}H_{33}N_5O_4$ 551	78	210
VIIan	2-Hydroxy-1-naphthyl	4-Antipyrinyl	$C_{34}H_{30}N_4O_5$ 574	72	200

*Solvent used for crystallization for all derivatives of *VII* is dioxane.

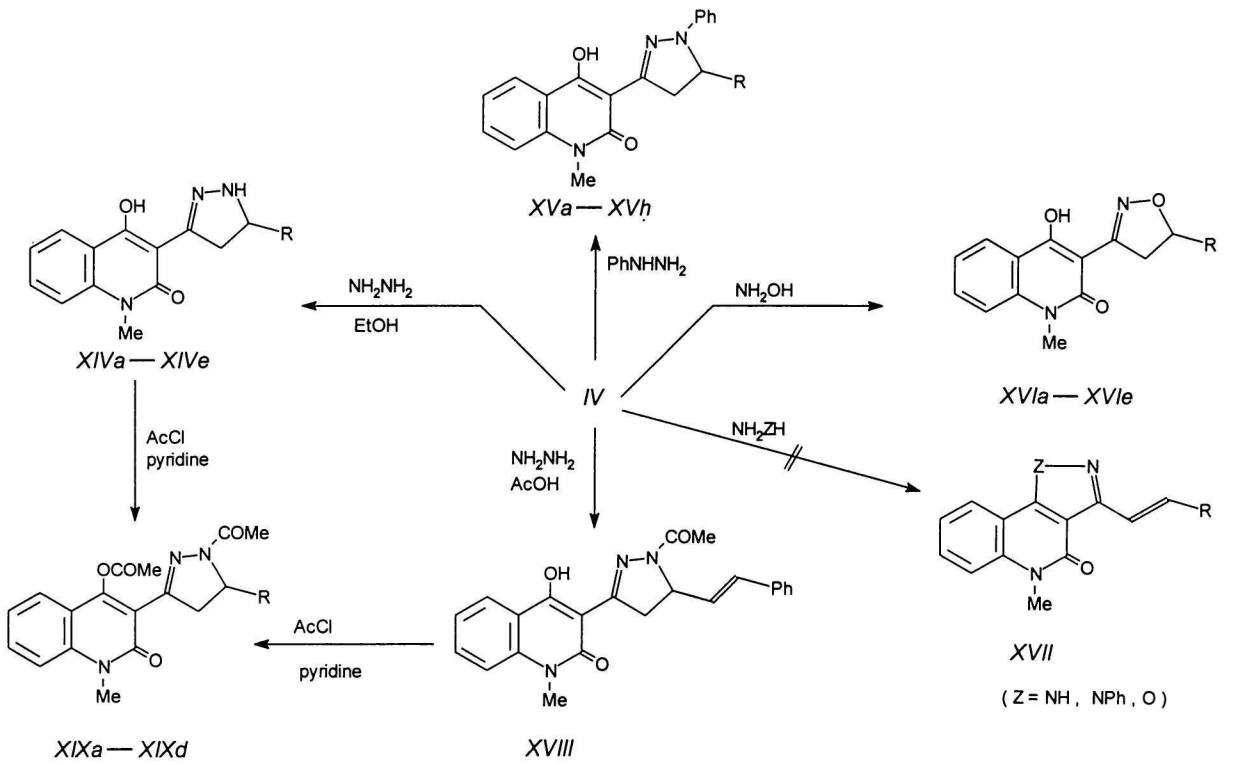


Scheme 2

acryloyl derivatives *IV* (R = 4-hydroxyphenyl, 3,4-methylenedioxyphenyl, 2-hydroxy-1-naphthyl, 4-nitrophenyl, 4-dimethylaminophenyl, 4-chlorophenyl, and 2-furyl) with some primary arylamines afforded the corresponding 3-(3-arylaminopropionyl)-2-quinolones *VIIa—VIIan*. The spectral and analytical data showed the presence of a carbonyl group in the side chain, and the consumption of the acryloyl (C=C) bond. The IR spectrum of compound *VIIa* showed ν(C=O) at $\tilde{\nu}$ = 1680 cm^{-1} which is characteristic of the side chain carbonyl group. The UV spectrum of this derivative revealed a hypsochromic shift of λ_{max} due to addition of the amine to the conjugated enone system which is no longer present in the afforded resultant *VIIa* and its analogues *VIIb—VIIan*. Similar results were obtained when reacting *IV* (R = 3,4-methylenedioxyphenyl, 2-hydroxy-1-naphthyl, and 4-dimethylaminophenyl) with diphenylamine; the 3-(3-

Table 3. Characterization of the Compounds *IX*—*XIII*

Compound	R or R′	Formula M_r	Yield %	M.p. °C	Solvent
IXa	4-Dimethylaminophenyl	$C_{33}H_{31}N_3O_3$ 517	85	99	Dioxane
IXb	3,4-Methylenedioxyphenyl	$C_{32}H_{26}N_2O_5$ 518	74	122	Dioxane
IXc	2-Hydroxy-1-naphthyl	$C_{35}H_{28}N_2O_4$ 540	80	130	Dioxane
X	Phenyl	$C_{25}H_{21}NO_3S$ 415	65	123	AcOH
XIa	4-Aminophenyl	$C_{27}H_{25}N_3O_3$ 439	69	190	Dioxane
XIb	8-Amino-1-naphthyl	$C_{31}H_{27}N_3O_3$ 489	78	182	Dioxane
XIc	1-Naphthyl	$C_{31}H_{26}N_2O_3$ 474	73	85	Dioxane
XId	4-Antipyrinyl	$C_{32}H_{30}N_4O_4$ 534	80	110	Dioxane
XIe	2,5-Dichlorophenyl	$C_{27}H_{22}N_2O_3Cl_2$ 493	81	148	Dioxane
XII		$C_{33}H_{28}N_2O_3$ 500	56	180	DMF
XIIIa	Ethyl	$C_{23}H_{23}NO_3S$ 393	71	105	CCl_4
XIIIb	4-Chlorophenyl	$C_{27}H_{22}NO_3ClS$ 475.5	75	115	CCl_4



Scheme 3

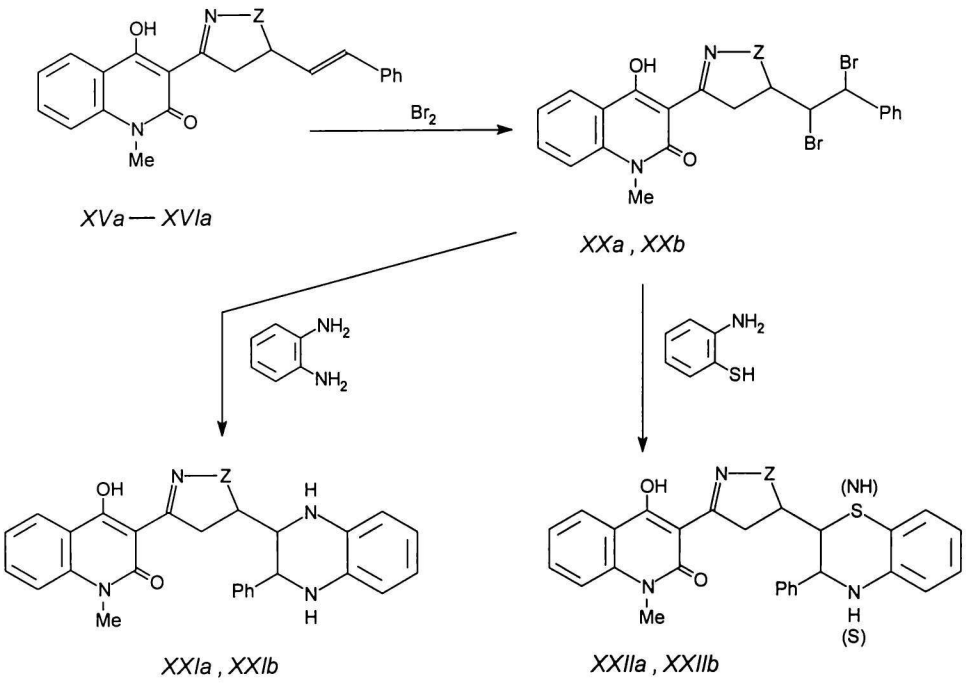
diphenylaminopropionyl)-2-quinolones *IXa*—*IXc* were the products obtained. Also, the addition reaction between thiophenol and *IV* (R = phenyl) was performed using triethylamine as a catalyst affording the sulfide *X*. Carrying out the latter addition reactions of primary and secondary aromatic amines and thiols

Table 4. Characterization of the Compounds *XIV*—*XXII*

Compound	R	Formula M_r	Yield %	M.p. °C	Solvent
XIVa	Styryl	$C_{21}H_{19}N_3O_2$ 345	83	196	Dioxane
XIVb	4-Chlorophenyl	$C_{19}H_{16}N_3O_2Cl$ 353.5	59	172	EtOH
XIVc	4-Dimethylaminophenyl	$C_{21}H_{22}N_4O_2$ 362	74	115	EtOH
XIVd	3,4-Methylenedioxyphenyl	$C_{20}H_{17}N_3O_4$ 363	81	166	EtOH
XIVe	2,5-Dimethylphenyl	$C_{21}H_{21}N_3O_2$ 347	67	169	Benzene
XVa	Styryl	$C_{27}H_{23}N_3O_2$ 421	66	206	EtOH
XVb	4-Chlorophenyl	$C_{25}H_{20}N_3O_2Cl$ 429.5	78	210	EtOH
XVc	4-Dimethylaminophenyl	$C_{27}H_{26}N_4O_2$ 438	83	244	EtOH
XVd	3,4-Methylenedioxyphenyl	$C_{26}H_{21}N_3O_4$ 439	80	180	EtOH
XVe	2,5-Dimethylphenyl	$C_{27}H_{25}N_3O_2$ 423	75	252	Benzene
XVf	2-Hydroxyphenyl	$C_{25}H_{21}N_3O_3$ 411	73	184	EtOH
XVg	2-Furyl	$C_{23}H_{19}N_3O_3$ 385	75	158	EtOH
XVh	2-Hydroxy-1-naphthyl	$C_{29}H_{23}N_3O_3$ 461	68	262	Anisole
XVIa	Styryl	$C_{21}H_{18}N_2O_3$ 346	56	240	Dioxane
XVIb	4-Chlorophenyl	$C_{19}H_{15}N_2O_3Cl$ 354.5	64	199	EtOH
XVIc	4-Dimethylaminophenyl	$C_{21}H_{21}N_3O_3$ 363	66	155	EtOH
XVIII		$C_{23}H_{21}N_3O_3$ 387	73	236	1-BuOH
XIXa	Styryl	$C_{25}H_{23}N_3O_4$ 429	75	198	AcOH
XIXb	4-Chlorophenyl	$C_{23}H_{20}N_3O_4Cl$ 437.5	81	154	EtOH
XIXc	4-Dimethylaminophenyl	$C_{25}H_{26}N_4O_4$ 446	64	122	EtOH
XIXd	3,4-Methylenedioxyphenyl	$C_{24}H_{21}N_3O_6$ 447	90	146	EtOH
XXa	N—Ph	$C_{27}H_{23}N_3O_2Br_2$ 581	76	285	DMF
XXb	O	$C_{21}H_{18}N_2O_3Br_2$ 506	71	178	Dioxane
XXIa	N—Ph	$C_{33}H_{29}N_5O_2$ 527	88	225	EtOH
XXIb	O	$C_{27}H_{24}N_4O_3$ 452	90	260	Dioxane
XXIIa	N—Ph	$C_{33}H_{28}N_4O_2S$ 544	60	142	MeOH
XXIIb	O	$C_{27}H_{23}N_3O_3S$ 469	80	155	MeOH

with 3-cinnamylidene acetylquinoline *IV* (R = styryl) gave the expected adducts: *XIa*—*XIe*, *XII*, and *XIIIa*, *XIIIb*, respectively, in which the addition involved the positions 4,5 of the conjugated diene ketone side chain. This was confirmed by the UV spectrum of compound *XIa*, from which it was obvious that addition of an arylamino group decreased the conjugation and consequently λ_{max} appeared at 380.3 nm, indicating that the increment of the conjugation of the side chain enone system, in λ_{max} due to the styryl group was no longer present (Scheme 2, Tables 2 and 3).

When the 3-acryloyl derivatives *IV* were allowed to react with hydrazine, phenylhydrazine, and hydroxylamine in ethanol, cyclocondensation products were



Scheme 4

obtained in fair yields, and identified as the pyrazolines *XIVa—XIVe*, 1-phenylpyrazolines *XVa—XVh*, and isoxazolines *XVIa—XVIc*. On the basis of the IR and ^{1}H NMR spectral data of the compounds *XIV—XVI* along with their analytical analyses, it was concluded that the cyclization is directed away from the OH group at position 4 of the quinoline. Also, the presence of the enolic OH group, as detected by the ferric chloride test and IR spectrum, and their found chemical shift sets characteristic of the Δ^2-pyrazoline ring system supported our proposed structures, and showed no evidences for formation of the diazolo[4,5-*c*]quinolines *XVII*. However, the reaction of *IVa* with hydrazine hydrate in the presence of acetic acid gave rise to the 3-(1-acetyl-5-styryl-3-pyrazolinyl)-2-quinolone *XVIII*. The structure of the compound *XVIII* was evidenced by analogy with other reported results in the literature [9, 10]. Moreover, acetylation of *XVIII*, using acetyl chloride in pyridine, yielded the 4-acetoxy-3-(1-acetyl-5-styryl-3-pyrazolinyl)-2-quinolone *XIXa*. The same product *XIXa* and its other analogues *XIXb—XIXd* were obtained on acetylation of the pyrazolines *XIVa—XIVd* (Scheme 3, Table 4).

Addition of bromine to the 3-(5-styryl-3-pyrazolinyl/isoxazolinyl)-2-quinolones *XVa*, *XVIa* readily gave the corresponding 1,2-dibromophenethyl derivatives *XXa*, *XXb*. Besides IR and ^{1}H NMR spectra of compound *XXa*, the mass spectrum showed additional evidences for its assigned structure revealing the presence of peaks at m/z 581, 583, and 585 due to M^+, $M^+ + 2$, and $M^+ + 4$ of relative abundance 1:2:1, respectively, characteristic of the presence of two bromine atoms. On reacting the latter products *XXa* and *XXb* with *o*-phenylenediamine or *o*-aminothiophenol two novel interesting heterotricyclic isolated systems were formed and characterized as the 3-(5-(2-quinoxalinyl)-3-pyrazolinyl/isoxazolinyl)-2-quinolones *XXIa*, *XXIb* and 3-(5-2/3-benzisothiazinyl)-3-pyrazolinyl/isoxazolinyl)-2-quinolones *XXIIa*, *XXIIb*, respectively (Scheme 4, Table 4).

EXPERIMENTAL

Melting points were determined in open capillary tubes and are uncorrected. Infrared spectra were recorded on a Perkin—Elmer 598 spectrophotometer using KBr disks. UV spectra were taken on a JASCO model V-550 UV VIS spectrophotometer. ^{1}H NMR spectra were taken on a Varian 390 EM spectrometer (90 MHz) and a Jeol FX 90 NMR spectrometer (90 MHz), using DMSO-d_6 as a solvent and TMS as an internal standard. Mass spectra were determined on a HP-5988 mass spectrometer by direct inlet (electron beam energy 70 eV). Characterization of the new compounds is given in Tables 1—4, all compounds gave satisfactory C, H, and N analyses within ± 0.4 % of the calculated ones.

3-(3-Arylacryloyl)- (*IVa—IVs*), 3-(2-Acetyl-3-arylacryloyl)- (*Va—Ve*), and 3-(3-Aryl-2-ethoxycarbonylacryloyl)-1,2-dihydro-4-hydroxy-1-methyl-2-quinolones (*VIa—VId*)

A mixture of *I*, *II*, and *III*, respectively (0.01 mol), the proper aldehyde (0.01 mol), and few drops of

piperidine was heated on a boiling water bath for 2—4 h. The reaction mixture was triturated with ethanol and the solid so obtained was filtered off, washed with diethyl ether, and crystallized.

IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$ (*IVa*): 1580—1600 ν(C=C), 1650 ν(C=$O_{quinolone}$), 1665 ν(C=$O_{acryloyl}$), 2600 ν(H-bonded OH). UV spectrum (acetone), λ_{max}/nm (*IVa*): 389.6. ^{1}H NMR spectrum (DMSO-d_6), δ (*IVa*): 3.55 (s, 3H, NCH_3), 6.50—6.95 (m, 4H, H_{olefin}), 7.05—8.16 (m, 9H, H_{arom}), 11.21 (bs, 1H, OH).

IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$ (*Va*): 1590—1610 ν(C=C), 1635 ν(C=$O_{quinolone}$), 1665, 1680 ν(C=$O_{acetoacryloyl}$), 2600 ν(H-bonded OH). ^{1}H NMR spectrum (DMSO-d_6), δ (*Va*): 2.51 (s, 3H, $COCH_3$), 3.56 (s, 3H, NCH_3), 6.35—6.62 (m, 3H, H_{olefin}), 7.07—8.09 (m, 9H, H_{arom}), 11.60 (bs, 1H, OH).

IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$ (*VIa*): 1585—1605 ν(C=C), 1642 ν(C=$O_{quinolone}$), 1670 ν(C=$O_{acryloyl}$), 1750, 1755 ν(C=O_{ester}), 2560 ν(H-bonded OH). ^{1}H NMR spectrum (DMSO-d_6), δ (*VIa*): 1.23 (t, 3H, $CO_2CH_2C\underline{H}_3$), 3.65 (s, 3H, NCH_3), 4.18 (q, 2H, $CO_2C\underline{H}_2CH_3$), 6.38—6.65 (m, 3H, H_{olefin}), 7.08—8.11 (m, 9H, H_{arom}), 11.65 (bs, 1H, OH).

3-(3-Aryl-3-arylaminopropionyl)- (*VIIa—VIIan*), 3-(3-Aryl-3-diphenylaminopropionyl)- (*IXa—IXc*), 3-(5-Arylamino-5-phenylpent-2-enoyl)- (*XIa—XIe*), and 3-(5-Diphenylamino-5-phenylpent-2-enoyl)-1,2-dihydro-4-hydroxy-1-methyl-2-quinolones (*XII*)

To a solution or suspension of the corresponding compounds *IV* (0.01 mol) in absolute ethanol (50 cm^3), the appropriate arylamine was added. The reaction mixture was heated under reflux for 4 h, then cooled to room temperature and the solid deposit so formed was filtered off and crystallized to give the corresponding adduct.

IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$ (*VIIa*): 1650 ν(C=$O_{quinolone}$), 1680 ν(C=$O_{propionyl}$), 2600—3180 ν(H-bonded OH), 3200—3580 (NH and phenolic OH). UV spectrum (acetone), λ_{max}/nm (*VIIa*): 369.7 ^{1}H NMR spectrum (DMSO-d_6), δ (*VIIa*): 3.45 (d, 2H, $COC\underline{H}_2CH$), 3.62 (s, 3H, NCH_3), 3.80—3.88 (m, 1H, $C\underline{H}NH$), 4.00 (s, 3H, OCH_3), 4.71 (bs, 1H, NH), 6.90—8.15 (m, 12H, H_{arom}), 11.72, 11.75 (bs, 2H, 2 × OH).

IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$ (*XIa*): 1650 ν(C=$O_{quinolone}$), 1665 ν(C=$O_{acryloyl}$), 2620 ν(H-bonded OH), 3280—3360, 3450 (NH and NH_2). UV spectrum (acetone), λ_{max}/nm (*XIa*): 380.3. ^{1}H NMR spectrum (DMSO-d_6), δ (*XIa*): 3.38 (dd, 2H, =CH—$C\underline{H}_2$—CHN), 3.62 (s, 3H, NCH_3), 3.90 (m, 1H, N—CHPh), 4.50 (d, 1H, NH), 4.65 (bs, 2H, NH_2), 6.50—6.72 (m, 1H, H_{olefin}), 6.93 (d, 1H, H_{olefin}), 7.08—8.20 (m, 13H, H_{arom}), 11.80 (bs, 1H, OH).

IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$ (*IXa*): 1650 ν(C=$O_{quinolone}$), 1685 ν(C=$O_{propionyl}$), 2620 ν(H-bonded OH). ^{1}H NMR spectrum (DMSO-d_6), δ (*IXa*): 2.25 (s, 6H, $N(CH_3)_2$), 3.40 (d, 2H, CH_2), 3.65 (s, 3H, NCH_3), 3.81 (t, ^{1}H, CH—N), 6.90—8.14 (m, 18H, H_{arom}), 11.45 (bs, 1H, OH).

IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$ (*XII*): 1648 ν(C=$O_{quinolone}$), 1665 ν(C=$O_{acryloyl}$), 2550 ν(H-bonded OH). ^{1}H NMR spectrum (DMSO-d_6), δ (*XII*): 2.75 (m, 2H, CH_2), 3.63 (s, 3H, NCH_3), 3.80 (t, 1H, CH—N), 5.95 (m, 1H, H_{olefin}), 6.82 (d, 1H, H_{olefin}), 6.95—8.21 (m, 19H, H_{arom}), 11.82 (bs, 1H, OH).

3-(3-Phenylthio-3-phenylpropionyl)-1,2-dihydro-4-hydroxy-1-methyl-2-quinolone (*X*) and 3-(5-Ethyl(4-chlorophenylthio)-5-phenylpent-2-enoyl)-1,2-dihydro-4-hydroxy-1-methyl-2-quinolones (*XIIIa, XIIIb*)

A mixture of each *IVp* and *IVa* (0.01 mol), the proper thiol (0.01 mol), and few drops of piperidine or triethylamine was heated on a boiling water bath for 4 h. The reaction mixture was cooled, triturated with diethyl ether and filtered off. The solid so obtained was crystallized from the suitable solvent.

IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$ (*X*): 1650 ν(C=$O_{quinolone}$), 1675 ν(C=$O_{propionyl}$), 2630 ν(H-bonded OH). ^{1}H NMR spectrum (DMSO-d_6), δ (*X*): 3.20 (d, 2H, CH_2CO), 3.65 (s, 3H, NCH_3), 3.85 (t, 1H, CH—S), 7.05—8.18 (m, 13H, H_{arom}), 11.55 (bs, 1H, OH). IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$ (*XIIIb*): 1585—1603 ν(C=C), 1650 ν(C=$O_{quinolone}$), 1663 ν(C=$O_{acryloyl}$), 2580—2620 ν(H-bonded OH). ^{1}H NMR spectrum (DMSO-d_6), δ(*XIIIb*): 1.81 (m, 2H, CH_2), 3.63 (s, 3H, NCH_3), 3.74 (t, 1H, CH—S), 5.45 (m, 1H, H_{olefin}), 6.55 (d, 1H, H_{olefin}), 6.95—8.13 (m, 13H, H_{arom}).

3-(5-Aryl-Δ^2-pyrazolin-3-yl)- (*XIVa—XIVe*) and 3-(5-Aryl-1-phenyl-Δ^2-pyrazolin-3-yl)-1,2-dihydro-4-hydroxy-1-methyl-2-quinolones (*XVa—XVh*)

To a solution or suspension of the compounds *IV* (0.01 mol) in ethanol (40 cm^3), hydrazine hydrate (0.01 mol) was added. The reaction mixture was refluxed for 5 h, then cooled and the deposit so obtained was filtered off and crystallized.

IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$ (*XIVa*): 1580—1600 ν(C=C), 1605—1618 ν(C=N), 1645 ν(C=O), 2625 ν(H-bonded OH), 3150—3200 (NH). ^{1}H NMR spectrum (DMSO-d_6), δ (*XIVa*): 3.22 (d, 2H, $CH_{2\ pyrazoline}$), 3.60 (s, 3H, NCH_3), 4.90 (m, 1H, $CH_{pyrazoline}$), 6.20—6.63 (m, 3H, H_{olefin} and $NH_{pyrazoline}$), 7.15—8.18 (m, 9H, H_{arom}), 11.75 (bs, 1H, OH).

IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$ (*XVa*): 1600 ν(C=C), 1610—1620 ν(C=N), 1660 ν(C=O), 2700 ν(H-bonded OH). ^{1}H NMR spectrum (DMSO-d_6), δ (*XVa*): 2.53 (d, 2H, $CH_{2\ pyrazoline}$), 3.65 (s, 3H, NCH_3), 4.65 (m, 1H, $CH_{pyrazoline}$), 6.20—6.55 (m, 2H, H_{olefin}), 7.03—8.10 (m, 14H, H_{arom}), 11.35 (bs, 1H, OH).

3-(5-Aryl-Δ^2-isoxazolin-3-yl)-1,2-dihydro-4-hydroxy-1-methyl-2-quinolones (*XVIa—XVIe*)

A mixture of *IV* (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 mixture was collected by filtration and crystallized.

IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$ (*XVIa*): 1600 ν(C=C), 1620 ν(C=N), 1655 ν(C=O), 2720—3100 ν(H-bonded OH). ^1H NMR spectrum (DMSO-d_6), δ (*XVIa*): 3.55 (d, 2H, $CH_{2\ isoxazoline}$), 3.62 (s, 3H, NCH_3), 4.81 (m, 1H, $CH_{isoxazoline}$), 6.21—6.84 (m, 2H, H_{olefin}), 7.10—8.05 (m, 9H, H_{arom}), 11.70 (bs, 1H, OH).

3-(1-Acetyl-5-styryl-Δ^2-pyrazolin-3-yl)-1,2-dihydro-4-hydroxy-1-methyl-2-quinolone (*XVIII*)

Refluxing a solution of *IVa* (0.005 mol) with hydrazine hydrate (0.005 mol) in glacial acetic acid (15 cm^3) for 8 h and cooling of the mixture gave a solid crystalline product.

IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$ (*XVIa*): 1590—1620 ν(C=C and C=N), 1645 ν($C=O_{quinoline}$), 1660 ν($C=O_{acetyl}$), 2620—2800 ν(H-bonded OH). ^1H NMR spectrum (DMSO-d_6), δ (*XVIa*): 2.23 (s, 3H, $COCH_3$), 2.90 (d, 2H, $CH_{2\ pyrazoline}$), 3.60 (s, 3H, NCH_3), 3.85 (m, 1H, $CH_{pyrazoline}$), 6.45—6.63 (m, 2H, H_{olefin}), 7.15—8.08 (m, 9H, H_{arom}), 11.38 (s, 1H, OH). Mass spectrum, m/z (I_r/%): 387 (45) (M^+), 372 (60) (M^+—CH_3), 344 (100) (M^+—$COCH_3$).

4-Acetoxy-3-(1-acetyl-5-aryl-Δ^2-pyrazolin-3-yl)-1,2-dihydro-1-methyl-2-quinolones (*XIXa—XIXd*)

A solution of compound *XIV* or *XVIII* (0.005 mol) in pyridine (15 cm^3) was dropwise treated with acetyl chloride (0.012 mol) with continuous stirring at room temperature. The mixture was then warmed to $\approx$ 60 °C for 15 min, cooled and poured into a cooled dilute hydrochloric acid (25 cm^3, w(HCl) = 10 %). The solid so formed was filtered, dried well, and crystallized.

IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$ (*XIXa*): 1585—1620 ν(C=C and C=N), 1640 ν($C=O_{quinoline}$), 1660 ν($C=O_{N\text{-}acetyl}$), 1750 ν($C=O_{O\text{-}acetyl}$). ^1H NMR spectrum (DMSO-d_6), δ (*XIXa*): 2.24 (s, 3H, $NCOCH_3$), 2.35 (s, 3H, $OCOCH_3$), 3.05 (d, 2H, $CH_{2\ pyrazoline}$), 3.65 (s, 3H, NCH_3), 3.85 (m, 1H, $CH_{pyrazoline}$), 6.45 (dd, 1H, H_{olefin}), 6.75 (d, 1H, H_{olefin}), 7.18—8.00 (m, 9H, H_{arom}).

3-(5-(1,2-Dibromophenethyl)-1-phenyl-Δ^2-pyrazolin/isoxazolin-3-yl)-1,2-dihydro-4-hydroxy-1-methyl-2-quinolones (*XXa, XXb*)

To a suspension of *XVa* resp. *XVIa* (0.01 mol) in carbon tetrachloride (25 cm^3) bromine (0.01 mol) was added with continuous stirring over 30 min. The crystalline yellow precipitate so formed was filtered, washed with chloroform (10 cm^3), dried, and crystallized.

IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$ (*XXa*): 1080 ν(C—Br), 1620 ν(C=N), 1645 ν(C=O), 2630 ν(H-bonded OH). ^1H NMR spectrum (DMSO-d_6), δ (*XXa*): 2.55 (d, 2H, $CH_{2\ pyrazoline}$), 3.65 (s, 3H, NCH_3), 3.93 (m, 1H, CH—N), 4.20 (dd, 1H, CHBr), 4.25 (d, 1H, CHBr), 7.00—8.08 (m, 14H, H_{arom}), 11.40 (bs, 1H, OH). Mass spectrum, m/z (I_r/%): 581 (12.1) (M^+), 583 (24) ($M^+ + 2$), 585 (11.60) ($M^+ + 4$), 503 (31.8) ($(M + 2)^+$—Br), 501 (32) (M^+—Br), 421 (65) (M^+—2Br), 419 (70) (M^+—2HBr), 340 (24), 239 (31), 316 (50), 206 (22), 199 (14), 174 (100), 132 (25), 103 (71), 92 (20), 77 (65).

3-(5-(3-Phenyl-1,2,3,4-tetrahydro-2-quinoxalinyl)-1,2-dihydro-4-hydroxy-1-methyl-1-phenyl-Δ^2-pyrazolin/isoxazolin-3-yl)-2-quinolones (*XXIa, XXIb*)

A mixture of *XXa* or *XXb* (0.01 mol) and *o*-phenylenediamine (0.01 mol) in ethanol (25 cm^3) containing pyridine (5 cm^3) was refluxed for 3 h. The reaction mixture was then cooled and poured into water, the solid deposit so obtained was collected by filtration, washed with methanol (10 cm^3), and crystallized.

IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$ (*XXIa*): 1610 ν(C=N), 1645 ν(C=O), 2600 ν(H-bonded OH), 3180—3240 ν(NH). ^1H NMR spectrum (DMSO-d_6), δ (*XXIa*): 2.45 (d, 2H, $CH_{2\ pyrazoline}$), 3.65 (s, 3H, NCH_3), 3.80—3.95 (m, 1H, CH—N), 5.60—5.73 (b, 2H, 2 × NH), 7.18—8.31 (m, 18H, H_{arom}), 11.83 (bs, 1H, OH).

3-(5-(2,3-Dihydro-3/2-phenyl-1,4-benzisothiazin-2/3-yl)-1-phenyl-Δ^2-pyrazolin/isoxazolin-3-yl)-1,2-dihydro-4-hydroxy-1-methyl-2-quinolones (*XXIIa, XXIIb*)

A mixture of *XXa* or *XXb* (0.01 mol), *o*-aminothiophenol (0.01 mol), and few drops of piperidine was heated on a boiling water bath for 4 h. The reaction mixture was then cooled, triturated with ethanol (10 cm^3) and the precipitate so formed was filtered and crystallized.

IR spectrum (KBr), $\tilde{\nu}/cm^{-1}$ (*XXIIa*): 1605 ν(C=N), 1653 ν(C=O), 2630 ν(H-bonded OH), 3180—3220 ν(NH). ^1H NMR spectrum (DMSO-d_6), δ (*XXIIa*): 2.60 (d, 2H, $CH_{2\ pyrazoline}$), 3.65 (s, 3H, NCH_3), 3.72 (dd, 1H, CH—$S_{thiazine}$), 5.90 (b, 1H, NH), 7.10—8.35 (m, 18H, H_{arom}), 11.85 (bs, 1H, OH).

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