New Quinolones and Naphthyridinones Bearing Heterocyclic Rings

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The behaviour of some α,β-unsaturated ketones or β-diketones, derived from quinolones, naphthyridinones or a combination of both of them, towards amines, diamines, and other ammonia derivatives at different ratios and conditions had been studied; the result were many interesting polyheterocyclic compounds containing either quinolone, naphthyridinone or both as the main moiety besides the recently formed hetero rings as: diazepine, oxazepine, thiazepine, triazepine, thiazole, thiazoline, pyrazoline, isooxazoline, pyrimidine, indole, triazinoindole, and quinoxaline. The structures of the resulting new polyheterocyclic compounds were established by chemical reactions, elemental analysis, and spectral data.

Quinolones and naphthyridinones are famous categories of compounds known by their intensive biological activity and vital important medicinal and pharmaceutical applications [1—4]. This prompted us long ago to carry out intensive research work on these classes of organic compounds [5—8].

In our previous publication [9] the action of primary amines on the 3-acryloyl-4-hydroxy-2-oxoquinoline *I* was studied at the mole ratio (x_r) 1:1, and the products were found to be the 1,4-Michael type adducts *II* (Scheme 1). In the present work the study is extended by carrying out the reaction at the mole ratio 2:1. The IR spectra of the products revealed the absence of the C═O absorption peak of the side chain, indicating that it is captured in the reaction course, which means that the reaction products are the amino-imino compounds *III*, where one molecule of the amine underwent Michael type addition, while the other condensed to the carbonyl side chain, many supports had been done for that result, among them is microelemental analysis, NMR spectral data and producing compound *III* directly from the reaction of compounds *II* with one mole of the same primary amine.

Diamines and other bifunctional reagents such as *o*-phenylenediamine, *o*-aminothiophenol, ethylenediamine, and ethanolamine, when subjected to react with the α,β-unsaturated ketones *I*, cycloaddition-condensation reaction took place giving rise to the novel heterocyclic compounds of expected biological importance: benzodiazepine *IV*, benzothiazepine *V*, diazepine *VIa* and oxazepine *VIb* derivatives, the structures of which found good supports from spectral data and elemental analysis.

The study of action of amines and diamino reagents was extended to the β-diketones *VII* [6] (Scheme 2), where primary, secondary, aliphatic, aromatic or heterocyclic amines condense with the ω-enolized carbonyl group to give the α,β-unsaturated oxoenamines *VIIIa*—*VIIIm*, these structures were inferred from their analytical and spectral data as well as similarity to the well-known reactions, cited in the literature [10]. The bifunctional amonia derivatives such as ethylenediamine, semicarbazide, thiosemicarbazide, and aminoguanidine furnished the diazepine *IX*, triazepinone, triazepinthione, and iminotriazepine *Xa*—*Xc*, respectively. The structures of these compounds were deduced from their correct elemental analysis and spectroscopic studies.

Insertion of heterocyclic rings, of known biological activity, such as thiazole, pyrazole, and pyrimidine to the quinolone moiety was achieved by reacting the acetyl compound *XI* (Scheme 3) with 2-cyanomethylbenzothiazole, 2-phenylimino-4-thiazolidinone, 3-methyl-5-pyrazolinone, 3-phenyl-5-pyrazolinone, and barbituric acid, where the carbonyl of the acetylquinolinone *XI* condenses with the active methylene of the reagents giving rise to the novel compounds *XII*—*XVI*, which are characterized by elemental analysis and their IR and ^{1}H NMR data are in good accordance with the suggested formula.

Reaction of the acetylquinolinone *XI* with some carbohydrazide derivatives produced new compounds *XVIIa*—*XVIId*, having the corresponding hydrazones as substituents to the quinolinone skeleton at position 3. These substituents may induce good pharmaceutical properties to the newly synthesized compounds. The acid hydrazides used were: cyanoacetylhydrazine, *p*-methoxybenzoylhydrazine, *p*-chlorobenzoylhydrazine, and *o*-carbohydrazinopyridine. The structures of the compounds *XVIIa*—*XVIId* were elucidated using different physical and chemical tools where the data

Scheme 1

of their elemental and spectral analysis are coincident with the proposed formula. In a similar manner the acetyl compound *XI* reacts with potassium hydrazinecarbodithioate to give potassium (3-acetyl-4-hydroxy-1-methyl-2(1*H*)-quinolone)hydrazonocarbodithioate *XVIII* (Scheme 4), the structure of which is found to be in agreement with spectral data and microanalysis. The quinoxaline substructure is one of heterocyclic systems known by its biological activity, suitable to be immersed as a substituent to quinolone; compound *XI* was reacted with 2,3-dihydrazinoquinoxaline at the mole ratio 1:1, where the product obtained was identified as the hydrazone *XIX*. The presence of the hydrazine substrate in *XIX* was checked up by its reaction with benzaldehyde, affording the dihydrazone compound *XX*, furthermore *XIX* is highly affected by glacial acetic acid, giving rise to its acetyl derivative *XXI*. Another new biologically promising quinolone substituted by further heterocyclic system was obtained by reacting the acetylquinolone *XI* with isatine-3-hydrazone to produce 4-hydroxy-1-methyl-3-(2′-oxo-1*H*-indol-3-ylidenehydrazonoacetyl)-2(1*H*)-quinolone *XXII*.

The knowledge of the serious medicinal importance of naphthyridinones [11] prompted us to synthesize new members of this class of compounds,

Scheme 2

where 3-formyl-4-hydroxy-1,8-naphthyridinone *XXIII* (Scheme 5) was prepared and used as starting material for the preparation of new naphthyridinone derivatives. Condensation of the aldehyde *XXIII* with different acetyl derivatives (such as acetophenones and acetylquinolones) gave rise to new α,β-unsaturated ketones, which in turn converted to new pyrazolines and isooxazolines when reacted with hydrazines and/or hydroxylamine. The reaction of *XXIII* with acetophenone and/or 4-*N*-acetylaminoacetophenone was carried out, at the mole ratio 1:1, in the presence of piperidine as catalyst to afford α,β-unsaturated ketones *XXIVa*, *XXIVb*.

Another interesting α,β-unsaturated ketone *XXV* derived by combination of both quinolone and naphthyridinone skeletons was achieved by reacting the acetoacetylquinolone *VII* with the formylnaphthyridinone *XXIII* in the presence of piperidine as catalyst.

To facilitate the following study of additive effect of linking quinolone and naphthyridinone moieties on the biological activity of the combine we had reacted the formylnaphthyridinone *XXIII* with 3-acetyl-1-butyl-4-hydroxy-2(1*H*)-quinolinone *XXVI* to give α,β-unsaturated ketone *XXVII*. Elemental analysis and spectral data of compound *XXVII* are coincident with the proposed structure. The effect of hydrazine on each of α,β-unsaturated compounds *XXIV*, *XXV*, and *XXVII* was studied. Thus treatment of

Scheme 3

compound *XXIVa* with hydrazine hydrate gave the pyrazoline *XXVIII*. Elemental analysis of the latter compound was found in good accordance with the predicted structure which is formed by condensation of one molecule of hydrazine with the carbonyl group followed by intermolecular addition to the α,β-double bond giving rise to the new pyrazolinylnaphthyridinone *XXVIII*.

As mentioned before *XXV* is considered as α,β-unsaturated ketone, therefore it was expected that *XXV* may react with hydrazine at the mole ratio 1:1 to produce the pyrazoline *XXIX* or *XXX*. The actual product was neither of them, it was found that it does not react any more with an extra amount of hydrazine, which means that all the active carbonyl groups had been consumed in the reaction with the first mole of hydrazine. Therefore, the structure proposed for the product is *XXXI*, which found supports by its correct elemental analysis, IR and ^{1}H NMR spectra. IR spectrum gave good indication for the pyrazole structure where the characteristic bands for the two (C═O) groups of the acetoacrylyl moiety disappeared. On the other hand, the α,β-unsaturated ketone derivative of the combined naphthyridinone-quinolinone *XXVII* underwent normal cyclocondensation with hydrazine to produce the pyrazoline derivative *XXXIIa* and similar cyclocondensation took place when *XXVII* reacted with phenylhydrazine and hydroxylamine to afford the phenylpyrazoline and isoxazoline *XXXIIb* and *XXXIIc*, respectively. The structures of compounds *XXXIIa, XXXIIb* were established on the basis of their correct elemental analyses and spectral data.

The reaction of the aldehyde *XXIII* with 2,3-dihydrazinoquinoxaline was studied at different mole ratios. It was found that when the reaction was carried out at the mole ratio 1:1, the product was found to be the monohydrazone *XXXIII*, while at the mole ratio (formyl:reagent) 2:1, the product was identified as the dihydrazone *XXXIV* (Scheme 6). The compounds *XXXIII* and *XXXIV* were characterized by their correct elemental analyses and spectral data.

A strong evidence for the correctness of the structure proposed for compound *XXXIII* was attained by its successful condensation with benzaldehyde to form benzalazino derivative *XXXV* indicating the presence of a free hydrazino group in *XXXIII*. The structure

Scheme 4

XXXV was inferred from its correct elemental analysis and its IR spectral data.

In order to have more and more of the biologically promising naphthyridinone derivatives, the aldehyde *XXIII* was reacted with some ammonia derivatives (some amines and acid hydrazides). Thus, *XXIII* was subjected to react with *p*-aminoacetophenone to produce the imine *XXXVI*, the structure of which was easily inferred from its correct elemental analysis as well as spectral data.

One more interesting naphthyridinone derivative *XXXVII* bearing multiaza hetero rings, was obtained by refluxing the aldehyde *XXIII* in ethanol with 3-hydrazino-1,2,4-triazinoindole. Structure *XXXVII* was supported by its correct elemental analysis and spectral data.

The formation of further derivatives of naphthyridinones was performed by reacting *XXIII* with some acid hydrazides, to give the corresponding acylhydrazones *XXXVIIIa*—*XXXVIIIe*, the structures of which were fortified by correct elemental analysis and studying their spectra.

EXPERIMENTAL

Melting points were determined in open capillary using Gallenkamp melting point apparatus MFB-595. Infrared spectra were recorded on a Perkin—Elmer 598 spectrophotometer using samples in KBr discs. ^{1}H NMR spectra were taken on a Jeol FX-90 NMR spectrometer (90 MHz) and a Varian EM-390 NMR spectrometer, using DMSO-d_6 as the solvent and TMS as the internal standard. Elemental microanalyses were performed at the Microanalytical Centre, Cairo University. All compounds gave satisfactory values for w_i(found) (i: C, H, N (Cl and S)) within ± 0.4 % of the calculated values. Characterizations of the new compounds are listed in Tables 1—6.

Scheme 5

3-(3-Aryl-3-arylamino-1-aryliminopropan-1-yl)-4-hydroxy-1-methyl(1*H*)-quinolin-2-ones *IIIa*—*IIIf*

Method A

To a solution or suspension of each of compounds *IIa*—*IIf* (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 that deposited was filtered off and recrystallized to give the corresponding products.

Scheme 6

Method B

A mixture of compound *I* (0.01 mol), the proper primary arylamine (0.02 mol), and one drop of piperidine was heated on boiling water bath for 2 h. The solid mass so formed was triturated with cold methanol (20 cm^3), filtered off and crystallized. IR spectrum (KBr), $\tilde{\nu}$(*IIIa*)/cm^{-1}: 1610 (C═N), 1650 (C═$O_{quinolone}$), 2700—3000 (OH), 3400—3600 (NH).

3-(2-Aryl-Δ^4-benzo[*b*]-1,5-diazepin-4-yl)-4-hydroxy-1-methyl(1*H*)-quinolin-2-ones *IVa*—*IVd* and 4-Hydroxy-1-methyl-3-(7-styryl-Δ^4-1,4-diazepine/1,4-oxazepin-5-yl)-(1*H*)-quinolin-2-ones *VIa* and *VIb*

To a solution of compound *I* (0.01 mol) in glacial acetic acid (5 cm^3) the appropriate amine was added. The reaction mixture was refluxed for 4 h, cooled and

Table 1. Characterization of the New Compounds *III*—*VI*

Compound	Yield	M.p.	Solvent
	%	°C	
IIIa	74	192	MeOH
IIIb	96	150	MeOH
IIIc	84	218	EtOH
IIId	73	180	EtOH
IIIe	68	146	EtOH
IIIf	77	171	Dioxane
IVa	72	258	Dioxane
IVb	76	220	Dioxane
IVc	82	249	Dioxane
IVd	81	186	Dioxane
V	71	130	Benzene
VIa	66	162	DMF
VIb	58	210	MeOH

Table 2. Characterization of the New Compounds *VIII*—*X*

Compound	Yield	M.p.	Solvent
	%	°C	
VIIIa	71	140	MeOH
VIIIb	69	192	EtOH
VIIIc	81	116	MeOH
VIIId	76	162	MeOH
VIIIe	72	204	EtOH
VIIIf	69	105	MeOH
VIIIg	82	179	EtOH
VIIIh	79	275	DMF
VIIIi	82	213	MeOH
VIIIj	77	167	AcOH
VIIIk	80	116	MeOH
VIIIl	78	182	EtOH
VIIIm	88	110	EtOH
IX	83	243	AcOH
Xa	77	> 300	AcOH
Xb	69	141	EtOH
Xc	78	254	MeOH

poured into water. The solid precipitate was filtered off and crystallized.

IR spectrum (KBr), $\tilde{\nu}(IVa)/\mathrm{cm}^{-1}$: 1605—1620 (C═$N_{\mathrm{diazepine}}$), 1645 (C═$O_{\mathrm{quinolone}}$), 2640 (H-bonded OH), 3150 (NH). ^{1}H NMR spectrum (DMSO-d_6), $\delta(IVa)$: 3.24 (d, 2H, $CH_{2\,\mathrm{diazepine}}$), 3.65 (s, 3H, NCH_3), 3.85—3.90 (m, 1H, $CH_{\mathrm{diazepine}}$), 4.82 (b, 1H, NH), 6.92—8.17 (m, 14H_{arom}), 11.70—11.75 (b, 2H, 2OH exchangeable with D_2O). IR spectrum (KBr), $\tilde{\nu}(IVa)/\mathrm{cm}^{-1}$: 1580—1600 (C═C), 1600—1615 (C═$N_{\mathrm{diazepine}}$), 1645 (C═$O_{\mathrm{quinolone}}$), 2625 (H-bonded OH), 3125—3250 (NH).

4-Hydroxy-1-methyl-3-(2-styryl-Δ^4-1,5-benzo-[*b*]thiazepin-4-yl)(1*H*)-quinolin-2-one (*V*)

Table 3. Characterization of the New Compounds *XII*— *XVI*

Compound	Yield	M.p.	Solvent
	%	°C	
XII	94	172	Dioxane
XIII	78	122	MeOH
XIV	77	172	MeOH
XV	93	134	MeOH
XVI	93	290	DMF

Table 4. Characterization of the New Compounds *XVII*—*XXII*

Compound	Yield	M.p.	Solvent
	%	°C	
XVIIa	77	274	AcOH
XVIIb	63	279	AcOH
XVIIc	88	238	Dioxane
XVIId	67	242	AcOH
XVIII	71	283	AcOH
XIX	89	231	Dioxane
XX	69	242	Dioxane
XXI	78	182	Dioxane
XXII	93	242	AcOH

Table 5. Characterization of the New Compounds

Compound	Yield	M.p.	Solvent
	%	°C	
XXIVa	66	210	DMF
XXIVb	63	300	DMF
XXV	58	252	DMF
XXVII	56	260	DMF
XXVIII	65	292	DMF
XXXI	60	272	MeOH
XXXIIa	65	292	DMF
XXXIIb	63	294	AcOH
XXXIIc	62	281	DMF

A suspension of the compound *I* (0.01 mol) in methanol (20 cm^3) was treated with *o*-aminothiophenol (0.01 mol) and one drop of piperidine, shaken for 15 min at room temperature. The solid product so obtained was filtered off, washed with diethyl ether (20 cm^3) and crystallized.

IR spectrum of compound *V* is nearly the same as that of *VI* with the exception of the last peak.

3-(3-Arylaminobut-2-enoyl)-4-hydroxy-1-methyl(1*H*)-quinolin-2-ones *VIIIa*—*VIIIm*

Table 6. Characterization of the New Compounds *XXXIII*—*XXXVIII*

Compound	Yield	M.p.	Solvent
	%	°C	
XXXIII	84	302	EtOH
XXXIV	70	278	DMF
XXXV	75	234	EtOH
XXXVI	62	305	DMF
XXXVII	85	270	DMF
XXXVIIIa	92	252	DMF
XXXVIIIb	90	240	MeOH
XXXVIIIc	78	255	DMF
XXXVIIId	75	291	Anisole
XXXVIIIe	78	200	DMF

A solution of the acetoacetyl derivative *VII* (0.02 mol) in ethanol (5 cm^3) was treated with the appropriate amine (0.02 mol) and kept at room temperature overnight. The crystalline solid deposited was filtered off and crystallized.

^{1}H NMR spectrum (DMSO-d_6), δ(*VIIIa*): 2.27 (d, 3H, CH_3—C═), 3.7 (s, 3H, N—CH_3), 5.7 (s, 1H, CH═C), 6.35—6.75 (m, 4H_{arom}), 7.1—7.8 (m, 4$H_{quinolone}$), 8.0 (b, 3H, NH_2 + NH exchangeable with D_2O), 11.7 (b, 1H, OH exchangeable with D_2O).

3-(7-Methyl-2,3-dihydro-1*H*-1,4-diazepin-5-yl)-4-hydroxy-1-methyl(1*H*)-quinolin-2-one (*IX*)

To a solution of the compound *VII* (0.01 mol) in ethanol (25 cm^3), ethylenediamine (0.01 mol) was added and the mixture was refluxed for 2 h. The solid that deposited was filtered off and crystallized to afford *IX*.

IR spectrum (KBr), $\tilde{\nu}$(*IX*)/cm^{-1}: 1590—1600 (C═C), 1620 (C═$N_{diazepine}$), 1640 (C═$O_{quinolone}$), 2925—3126 (H-bonded OH), 3150—3300 (NH).

3-(7-Methyl-3-oxo-, -thioxo- or -imino-2,3-dihydro-1*H*-1,2,4-triazepin-5-yl)-4-hydroxy-1-methyl(1*H*)-quinolin-2-one *Xa*—*Xc*

A mixture of the acetoacetyl derivative *VII* (0.01 mol) and semicarbazide, thiosemicarbazide or aminoguanidine (0.012 mol) in ethanol (30 cm^3) was refluxed on a water bath for 2 h.The yellowish solid that formed was filtered off and crystallized to give *Xa*—*Xc*.

IR spectrum (KBr), $\tilde{\nu}$(*Xb*)/cm^{-1}: 1215—1340 (C═S), 1575 (C═$N_{triazepine}$), 1625 (C═$O_{quinoIone}$), 2550 (H-bonded OH), 3230 (NH). ^{1}H NMR spectrum (DMSO-d_6), δ(*Xa*): 2.10 (s, 3H, CH_3), 3.70 (s, 3H, NCH_3), 3.85—3.95 (m, 1H, $CH_{diazepine}$), 7.10—8.00 (m, 4H, H_{arom}), 10.70—11.00 (b, 2H, 2NH exchangeable with D_2O), 11.6 (b, 1H, OH exchangeable with D_2O).

2-(2-Benzothiazolyl)-3-methyl-3-(4-hydroxy-1-methyl-2-oxo(1*H*)-quinolin-3-yl)acrylonitrile (*XII*)

A mixture of the acetyl derivative *XI* (0.01 mol), 2-cyanomethylbenzothiazole (0.01 mol), and few drops 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.

IR spectrum (KBr), $\tilde{\nu}$(*XII*)/cm^{-1}: 720 (cyclic C—S—C), 1600 (C═C), 1620 (C═N), 1650 (C═$O_{quinolone}$), 2210 (C≡N), 2650—2930 (H-bonded OH). ^{1}H NMR spectrum (DMSO-d_6), δ(*XII*): 2.5 (s, 3H, CH_3), 3.65 (s, 3H, NCH_3), 7.12—8.15 (m, 8H, H_{arom}), 10.85 (b, 1H, OH exchangeable with D_2O).

5-[1-(4-hydroxy-1-methyl-2-oxo(1*H*)-quinolin-3-yl)ethylidene]-2-phenyliminothiazolidin-4-one (*XIII*)

Similar method to that used to obtain *XII* was followed using 2-phenyliminothiazolidin-4-one with the acetyl derivative *XI*.

IR spectrum (KBr), $\tilde{\nu}$(*XIII*)/cm^{-1}: 1180, 1200, 1330 (N═C—S), 1600 (C═C), 1620 (C═N), 1650 (C═$O_{quinolone}$), 1700 (C═$O_{thiazolidinone}$), 2620—3200 (H-bonded OH), 3150 (NH). ^{1}H NMR spectrum (DMSO-d_6), δ(*XIII*): 2.5 (s, 3H, CH_3), 3.70 (s, 3H, NCH_3), 7.2—8.00 (m, 9H, H_{arom}), 9.80 (b, 1H, NH exchangeable with D_2O), 10.85 (b, 1H, OH exchangeable with D_2O).

4-[1-(4-Hydroxy-1-methyl-2-oxo(1*H*)-quinolin-3-yl)ethylidene]-3-methyl/phenylpyrazolin-5-one *XIV* and *XV*

A procedure similar to that used for compound *XII* was utilized to obtain *XIV* and *XV* from the acetyl derivative *XI* with 3-methyl or -phenylpyrazolinones.

5-[1-(4-Hydroxy-1-methyl-2-oxo(1*H*)-quinolin-3-yl)ethylidene]barbituric Acid (*XVI*)

The above compound was prepared from compound *XI* and barbituric acid using the same method described for the synthesis of compound *XII*.

3-Aroylhydrazonoacetyl-4-hydroxy-1-methyl-(1*H*)-quinolin-2-ones *XVIIa*—*XVIId*

To a solution of the acetyl derivative *XI* (0.01 mol) in ethanol (25 cm^3) the appropriate acid hydrazide (cyanoacetylhydrazine, *p*-methoxybenzoylhydrazine, *p*-chlorobenzoylhydrazine or 2-pyridylcarbohydrazine) (0.01 mol) was added. The reaction mixture was then heated under reflux for 2 h and the solid deposited was filtered off and crystallized.

IR spectrum (KBr), $\tilde{\nu}$(*XVIIa*)/cm^{-1}: 1610 (C═N), 1650 (C═O$_{quinolone}$), 1760 (C═O$_{cyanoacetyl}$), 2257 (CN), 2800—3000 (H-bonded OH), 3220 (NH). ^{1}H NMR spectrum (DMSO-d_6), δ(*XVIIa*): 2.30 (s, 3H, CH_3), 3.56 (s, 3H, NCH_3), 6.49 (s, 2H, $COCH_2CN$), 7.00—8.00 (m, 4H, H_{arom}), 9.40 (b, 1H, NH exchangeable with D_2O), 11.45 (b, 1H, OH exchangeable with D_2O).

Potassium 3-[1-(4-Hydroxy-1-methyl-2-oxo-(1*H*)-quinolin-3-yl)ethylidene]hydrazinecarbodithioate (*XVIII*)

A solution of the acetyl derivative *XI* (0.01 mol) in ethanol (25 cm^3) was treated with potassium hydrazinecarbodithioate (0.01 mol), and the mixture was refluxed for 2 h on a water bath. The separated organic solid mass was filtered off and recrystallized affording compound *XVIII*.

IR spectrum (KBr), $\tilde{\nu}$(*XVIII*)/cm^{-1}: 660 (C—S—C), 1190—1270 (NHC═S), 1525, 1565 (CN), 1595, 1620 (C═N), 1635—1650 (C═O$_{quinolone}$), 2600—2750 (H-bonded OH), 3220 (NH). ^{1}H NMR spectrum (DMSO-d_6), δ(*XVIII*): 2.30 (s, 3H, NC—CH_3), 3.56 (s, 3H, NCH_3), 7.10—8.30 (m, 4H, H_{arom}), 9.30 (b, 1H, NH exchangeable with D_2O), 11.20 (b, 1H, OH exchangeable with D_2O).

3-(3-Hydrazino-2-quinoxalinylhydrazono)-acetyl-4-hydroxy-1-methyl(1*H*)-quinolin-2-one (*XIX*)

A mixture of *XI* (0.01 mol) and 2,3-dihydrazinoquinoxaline (0.01 mol) in ethanol (10 cm^3) was refluxed for 2 h. The yellow precipitate that formed was filtered off and crystallized to give *XIX*.

IR spectrum (KBr), $\tilde{\nu}$(*XIX*)/cm^{-1}: 1610 (C═N), 1645 (C═O$_{quinolone}$), 2500—3190 (b, NH and OH), 3284 (NH_2). ^{1}H NMR spectrum (DMSO-d_6), δ(*XIX*): 2.60 (s, 3H, NC—CH_3), 3.50 (s, 3H, NCH_3), 4.30 (s, 2H, NH_2 exchangeable with D_2O), 7.00—8.10 (m, 8H, H_{arom}), 9.30—9.60 (b, 2H, NH exchangeable with D_2O), 10.80 (b, 1H, OH exchangeable with D_2O).

3-(3-Benzalhydrazino-2-quinoxalinyl-hydrazono)acetyl-4-hydroxy-1-methyl(1*H*)-quinolin-2-one (*XX*)

Using the same method as for preparation of *XIX*, treatment of compound *XIX* with benzaldehyde yielded the compound *XX*.

3-[(3-Acetylhydrazino-2-quinoxalinyl-hydrazono)acetyl]-4-hydroxy-1-methyl(1*H*)-quinolin-2-one (*XXI*)

Compound *XIX* (0.005 mol) was dissolved in glacial acetic acid (25 cm^3) and heated under reflux for 4 h and left to cool to room temperature. The crystallized material so obtained was filtered off and washed with absolute ethanol (5 cm^3) and diethyl ether (20 cm^3).

4-Hydroxy-1-methyl-3-(2-oxoindol-3-ylidene)-hydrazonoacetyl(1*H*)-quinolin-2-one (*XXII*)

A solution of the acetyl derivative *XI* (0.01 mol) in ethanol (25 cm^3) was treated with isatine-3-hydrazone (0.01 mol) and the mixture was refluxed for 2 h on a water bath. The separated organic solid mass was filtered off and recrystallized affording compound *XXII*.

IR spectrum (KBr), $\tilde{\nu}$(*XXII*)/cm^{-1}: 1610 (C═N), 1675 (C═O$_{quinolone}$), 1690—1710 (C═O$_{indolinone}$), 2650—2700 (H-bonded OH), 3120—3200 (NH). ^{1}H NMR spectrum (DMSO-d_6), δ(*XXII*): 2.55 (s, 3H, NCH_3), 3.56 (s, 3H, NCH_3), 7.10—8.50 (m, 8H, H_{arom}), 11.00 (b, 1H, NH exchangeable with D_2O), 11.85 (b, 1H, OH exchangeable with D_2O).

3-(4-R-phenacylidene)methyl-4-hydroxy-1,8(1*H*)-naphthyridin-2-ones *XXIVa, XXIVb*

A mixture of the aldehyde *XXIII* (0.01 mol), acetophenone, resp. *p*-acetylaminoacetophenone, and one drop of piperidine was heated at 90 ℃ for 4 h. The reaction mixture was then cooled, triturated with methanol (10 cm^3), and the formed deposits were filtered off, washed with diethyl ether and crystallized.

IR spectrum (KBr), $\tilde{\nu}$(*XXIVa*)/cm^{-1}: 1600 (C═C), 1630 (C═O$_{quinolone}$), 1700 (C═O$_{side\ chain}$), 2500 (H-bonded OH), 3218 (NH). ^{1}H NMR spectrum (DMSO-d_6), δ(*XXIVa*): 6.2 (d, 2H, CH═CH), 7.10—8.30 (m, 8H, H_{arom}), 8.90 (s, 1H, NH exchangeable with D_2O), 11.60 (s, 1H, OH exchangeable with D_2O).

3-[3-(4-Hydroxy-2-oxo-1-methyl(1*H*)-quinoline-3-carbonyl)-2-oxo-3-buten-4-yl]-4-hydroxy-1,8(1*H*)-naphthyridin-2-one (*XXV*) and 1-Butyl-3-[β-(4-hydroxy-2-oxo-1,8(1*H*)-naphthyridin-3-yl)-acryloyl]-4-hydroxy(1*H*)-quinolin-2-one (*XXVII*)

A procedure similar to that described for compound *XXIV* was utilized to obtain compounds *XXV* and *XXVII* from the aldehyde *XXIII* and 3-acetoacetylquinolinone *VII* resp. 3-acetylquinolinone *XXVI*.

IR spectrum (KBr), $\tilde{\nu}$(*XXV*)/cm^{-1}: 1600 (C═C), 1635 (C═O$_{naphthyridinone}$), 1650 (C═O$_{quinolinone}$), 1730 (C═O$_{\alpha,\beta\text{-unsat.}}$), 2900—3000 (H-bonded OH), 3286 (NH). ^{1}H NMR spectrum (DMSO-d_6), δ(*XXV*): 2.40 (s, 3H, $COCH_3$), 3.80 (s, 3H, NCH_3), 6.50—6.70 (s, 1H, CH═C), 7.50—8.90 (m, 7H, H_{arom}), 9.2 (s, 1H, NH), 11.80 (b, 2H, 2OH exchangeable with D_2O).

IR spectrum (KBr), $\tilde{\nu}$(*XXVII*)/cm^{-1}: 1590—1610 (C═C), 1630 (C═O$_{naphthyridinone}$), 1650

(C═$O_{quinolinone}$), 1700 (C═$O_{\alpha,\beta\text{-unsat.}}$), 2600—2900 (H-bonded OH), 3280 (NH). ^{1}H NMR spectrum (DMSO-d_6), δ(*XXVII*): 0.91 (t, 3H, CH_3), 1.32—1.81 (m, 4H, $2CH_2$), 4.40 (t, 2H, α-CH_2), 6.20—6.52 (m, 2H, CH═CH), 7.05—8.16 (m, 7H, H_{arom}), 9.10 (s, 1H, NH exchangeable with D_2O), 11.20 (b, 2H, 2OH exchangeable with D_2O).

4-Hydroxy-2-oxo-3-(3-phenyl-Δ^2-pyrazolin-5-yl)-1,8(1*H*)-naphthyridine (*XXVIII*)

A suspension of the compound *XXIVa* (0.01 mol) in absolute ethanol (30 cm^3) containing DMF (5 cm^3) was treated with hydrazine hydrate (0.012 mol). The reaction mixture was heated under reflux for 2 h, then cooled and filtered off. The solid so obtained was crystallized to give compound *XXVIII*.

IR spectrum (KBr), $\tilde{\nu}$(*XXVIII*)/cm^{-1}: 1618 (C═N), 1627 (C═O), 2800 (H-bonded OH), 3480 (NH). ^{1}H NMR spectrum (DMSO-d_6), δ(*XXVIII*): 4.21 (b, 1H, $NH_{pyrazoline}$ exchangeable with D_2O), 6.21 (d, 2H, $CH_{2\,pyrazoline}$), 7.23—8.13 (m, 8H, H_{arom}), 8.6 (s, 1H, NH exchangeable with D_2O), 10.50 (b, 1H, OH exchangeable with D_2O).

3-(4-Hydroxy-1-methyl-2-oxo(1*H*)-quinolin-3-yl)-4-(4-hydroxy-2-oxo-1,8(1*H*)-naphthyridine-3-methylene)-5-methylpyrazole (*XXXI*) and 3-(1-Butyl-4-hydroxy-2-oxo(1*H*)-quinolin-3-yl)-5-(4-hydroxy-2-oxo-1,8(1*H*)-naphthyridin-3-yl)-Δ^2-pyrazolines or -Δ^2-isooxazoline *XXXIIa*—*XXXIIc*

A mixture of the compound *XXV* (0.01 mol) and hydrazine hydrate (0.012 mol) in absolute ethanol (25 cm^3) was refluxed for 3 h. The reaction mixture was then cooled and poured into cold water. The solid so obtained was filtered off, washed with cold methanol (15 cm^3) and crystallized.

IR spectrum (KBr), $\tilde{\nu}$(*XXXI*)/cm^{-1}*:* 1600 (C═C), 1614 (C═N), 1630 (C═$O_{naphthyridinone}$), 1645 (C═$O_{quinolinone}$), 2600—2900 (H-bonded OH), 3156 (NH). ^{1}H NMR spectrum (DMSO-d_6), δ(*XXXI*): 2.65 (s, 3H, CH_3), 3.65 (s, 3H, NCH_3), 6.20 (s, 1H, CH═C), 7.10—8.32 (m, 7H, H_{arom}), 8.85 (b, 1H, NH exchangeable with D_2O), 10.85—11.05 (b, 2H, 2OH exchangeable with D_2O).

IR spectrum (KBr), $\tilde{\nu}$(*XXXIIa*)/cm^{-1}: 1375 ($CH_{pyrazoline}$), 1624 (C═N), 1630 (C═$O_{naphthyridinone}$), 1650 (C═$O_{quinolinone}$), 2500—3200 (NH and H-bonded OH). ^{1}H NMR spectrum (DMSO-d_6), δ(*XXXIIa*): 0.95 (t, 3H, $CH_{3\,butyl}$), 1.65—1.82 (m, 4H, $2CH_{2\,butyl}$), 4.15 (t, 1H, $CH_{pyrazoline}$), 4. 43 (t, 2H, $NCH_{2\,butyl}$), 6.32 (d, 2H, $CH_{2\,pyrazoline}$), 6.50 (b, 1H, $NH_{pyrazoline}$ exchangeable with D_2O), 7.15—8.12 (m, 7H, H_{arom}), 8.50 (b, 1H, $NH_{naphthyridine}$ exchangeable with D_2O), 10.95—11.02 (b, 2H, 2OH exchangeable with D_2O).

4-Hydroxy-2-oxo-1,8(1*H*)-naphthyridine-3-carbaldehyde 3-Hydrazinoquinoxalin-2-yl-hydrazone (*XXXIII*) and Bis-(4-hydroxy-2-oxo-1,8(1*H*)-naphthyridine-3-carbaldehyde)-quinoxaline-2,3-diylhydrazone (*XXXIV*)

A mixture of the aldehyde *XXIII* (0.01 mol) and 2,3-dihydrazinoquinoxaline (0.01 mol) in absolute ethanol (10 cm^3) was refluxed for 2 h. The solid product that formed after cooling was filtered off, washed with cold methanol and crystallized to give *XXXIII*.

IR spectrum (KBr), $\tilde{\nu}$(*XXXIII*)/cm^{-1}: 1610 (C═N), 1630 (C═$O_{naphthyridinone}$), 2500—3200 (NH and H-bonded OH), 3290 (NH_2). ^{1}H NMR spectrum (DMSO-d_6), δ(*XXXIII*): 4.50 (s, 2H, NH_2 exchangeable with D_2O), 7.18—8.10 (m, 7H, H_{arom}), 8.52 (s, 1H, $CH_{azomethine}$), 8.95—9.30 (b, 3H, 3NH exchangeable with D_2O), 11.03 (b, 1H, OH exchangeable with D_2O).

Similarly compound *XXXIV* was obtained using the aldehyde *XXIII* (0.01 mol) and 2,3-dihydrazinoquinoxaline (0.005 mol), and the reaction was carried out under the same conditions.

IR spectrum (KBr), $\tilde{\nu}$(*XXXIV*)/cm^{-1}: 1610—1615 (C═N), 1635 (C═$O_{naphthyridinone}$), 2500—3100 (NH and H-bonded OH). ^{1}H NMR spectrum (DMSO-d_6), δ(*XXXIV*): 7.18—8.15 (m, 10H, H_{arom}), 8.52 (s, 1H, $CH_{azomethine}$), 8.90—9.19 (b, 4H, 4NH exchangeable with D_2O), 11.23 (b, 2H, 2OH exchangeable with D_2O).

4-Hydroxy-2-oxo-1,8(1*H*)-naphthyridine-3-carbaldehyde 3-Benzalhydrazinoquinoxalin-2-ylhydrazone (*XXXV*)

To a suspension of compound *XXXIII* (0.005 mol) in methanol (25 cm^3) benzaldehyde (0.005 mol) was added and the reaction mixture was refluxed for 1 h.The mixture was left to cool to room temperature and the precipitate so obtained was collected by filtration, washed thoroughly with cold methanol (10 cm^3) and crystallized.

IR spectrum (KBr), $\tilde{\nu}$(*XXXV*)/cm^{-1}: 1600—1620 (C═N), 1635 (C═$O_{naphthyridinone}$), 2600—3100 (NH and H-bonded OH).

3-(4-Acetylphenylimino)methyl-4-hydroxy-1,8(1*H*)-naphthyridin-2-one (*XXXVI*)

A mixture of the aldehyde *XXIII* (0.01 mol) and 4-aminoacetophenone (0.01 mol) in absolute ethanol (10 cm^3) was warmed at 55—60 °C for 2 h, then the reaction mixture was left to cool to room temperature and the solid so resulted was filtered off, dried and crystallized to give the imine *XXXVI*.

IR spectrum (KBr), $\tilde{\nu}$(*XXXVI*)/cm^{-1}: 1610 (C═N), 1629 (C═$O_{naphthyridinone}$), 1675 (C═O_{acetyl}), 2500—2700 (H-bonded OH).

4-Hydroxy-2-oxo-1,8(1*H*)-naphthyridine-3-carbaldehyde 5*H*-1,2,4-Triazino[5,6-*b*]indol-3-ylhydrazone (*XXXVII*)

A mixture of the aldehyde *XXIII* (0.01 mol) and 3-hydrazino-1,2,4(5*H*)-triazino[5,6-*b*]indole (0.01 mol) in ethanol (50 cm^3) containing DMF (5 cm^3) was refluxed for 4 h. The solid mass that formed was filtered off, washed thoroughly with cold ethanol (10 cm^3) and recrystallized.

IR spectrum (KBr), $\tilde{\nu}$(*XXXVII*)/cm^{-1}: 1610 (C═N), 1630 (C═$O_{naphthyridinone}$), 2500—2773 (H-bonded OH), 3080, 3110, 3200 (NH). ^{1}H NMR spectrum (DMSO-d_6), δ(*XXXVII*): 7.32—8.12 (m, 7H, H_{arom}), 8.61 (s, 1H, $CH_{azomethine}$), 8.90 (s, 1H, $NH_{naphthyridine}$ exchangeable with D_2O), 9.80 (s, 1H, $NH_{hydrazone}$ exchangeable with D_2O), 11.25 (s, 1H, NH_{indole} exchangeable with D_2O), 11.65 (s, 1H, OH exchangeable with D_2O).

4-Hydroxy-2-oxo-1,8(1*H*)-naphthyridine-3-carbaldehyde Acyl/Aroylhydrazones *XXXVIIIa*—*XXXVIIIe*

To a suspension of the aldehyde *XXIII* (0.01 mol) in ethanol (25 cm^3) the appropriate acylhydrazide (namely cyanoacetylhydrazide, 4-methoxybenzoylhydrazide, 2-*N*-phenyluriedobenzoylhydrazide, 4-chlorobenzoylhydrazide, 2,4-dichlorobenzoylhydrazide) (0.01 mol) was added and the reaction mixture was heated under reflux for 2 h. The solid deposits were filtered off and crystallized to give *XXXVIIIa*—*XXXVIIIe*.

IR spectrum (KBr), $\tilde{\nu}$(*XXXVIIIa*)/cm^{-1}: 1608 (C═N), 1629 (C═$O_{naphthyridinone}$), 2229 (C≡N), 2500—3200 (b, NH and H-bonded OH). ^{1}H NMR spectrum (DMSO-d_6), δ(*XXXVIIIa*): 6.47 (s, 2H, $COCH_2CN$), 7.00—8.20 (m, 3H, H_{arom}), 8.80 (s, 1H, $NH_{naphthyridine}$ exchangeable with D_2O), 9.50 (s, 1H, $NH_{acylhydrazone}$ exchangeable with D_2O), 11.50 (b, 1H, OH exchangeable with D_2O).

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