

HETEROCYCLES, Vol. 100, No. 7, 2020, pp. 1048 - 1064. © 2020 The Japan Institute of Heterocyclic Chemistry
Received, 24th April, 2020, Accepted, 15th May, 2020, Published online, 19th May, 2020
DOI: 10.3987/COM-20-14270

REACTIVITY OF 6-ETHYL-4,5-DIOXO-5,6-DIHYDRO-4H-PYRANO-[3,2-*c*]QUINOLINE-3-CARBOXALDEHYDE TOWARDS SOME NUCLEOPHILIC REAGENTS

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Abstract – 6-Ethyl-4,5-dioxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinoline-3-carboxaldehyde (**1**) was prepared and utilized as a starting material. Carboxaldehyde **1** was subjected to react with a diversity of carbon nucleophiles producing a variety of condensation products as well as heterocyclic rings linked pyrano[3,2-*c*]quinolines. Also, reaction of carboxaldehyde **1** with *p*-toluidine, heterocyclic amines and some hydrazine derivatives produced a variety of products. The structures of the new synthesized products were deduced on the basis of their analytical and spectral data.

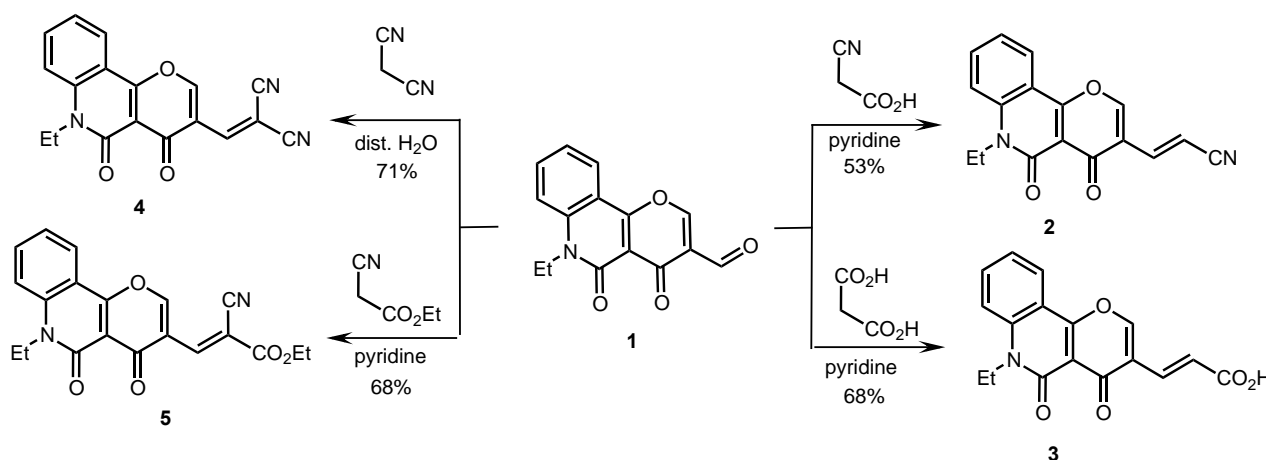
INTRODUCTION

Quinolines are important class of biologically active heterocyclic compounds¹ and several of their derivatives have been used as bactericidal,² antifungal,³ antimalarial,⁴ antitumor,⁵ antioxidant,⁶ antileishmanial⁷ and antiplatelet activities.⁸ In addition, these compounds showed important cytological,⁹ antiproliferative, antitubulin¹⁰ and anti-Alzheimer activities.¹¹ Also, different 4-hydroxyquinolin-2(1*H*)-ones revealed antiparasitic, molluscicidal, and larvicidal activities.¹² Moreover, pyrano[3,2-*c*]quinolines were examined for their electrical, optical, and photoelectrical properties.¹³ DFT calculations, quantum chemical studies, and electronic absorption spectra were studied with some pyrano[3,2-*c*]quinolines.¹⁴ Functionalized pyrano[3,2-*c*]quinolines were efficiently utilized for construction of heteroannulated pyrano[3,2-*c*]quinolines as well as quinolin-2(1*H*)-ones bearing variable heterocyclic rings.¹⁵ The title aldehyde, 6-ethyl-4,5-dioxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinoline-3-carboxaldehyde (**1**), was previously synthesized and its chemical reactivity was studied towards hydroxylamine hydrochloride under different reaction conditions.¹⁶ Herein, the aldehyde **1** was utilized as a starting compound hoping

to obtain new members of fused and isolated heterocyclic derivatives of quinolin-2-one family *via* its reaction with a variety of carbon and nitrogen nucleophilic reagents.

RESULTS AND DISCUSSION

In the previous work,¹⁶ a convenient synthesis of 6-ethyl-4,5-dioxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]-quinoline-3-carboxaldehyde (**1**) was achieved. The structure of aldehyde **1** contains variable electron-deficient centers and it is expected to be quite reactive towards nucleophilic reagents. Therefore, treatment of aldehyde **1** with cyanoacetic acid, in boiling pyridine, produced *E*-acrylonitrile derivative **2** (Scheme 1). It is thought that the reaction takes place initially *via* condensation reaction, with subsequent decarboxylation (Scheme 1).¹⁷ The mass spectrum of acrylonitrile **2** showed the molecular ion peak at m/z 292 which agrees with its molecular formula mass. The IR spectrum of acrylonitrile **2** displayed characteristic absorption band assigned to the nitrile function ($C\equiv N$) at 2204 cm^{-1} . The ^1H NMR spectrum of compound **2** exhibited two characteristic doubles at δ 8.68 and 9.07 ($J=13.8\text{ Hz}$), confirming *E*-configuration of the product **2**. The ^{13}C NMR spectrum of compound **2** showed two distinctive signals attributed to $C\equiv N$ and $C=O_{\gamma\text{-pyrone}}$ at δ 116.8 and 178.6 ppm, respectively.



Scheme 1. Condensation of aldehyde **1** with some acyclic active methylene compounds

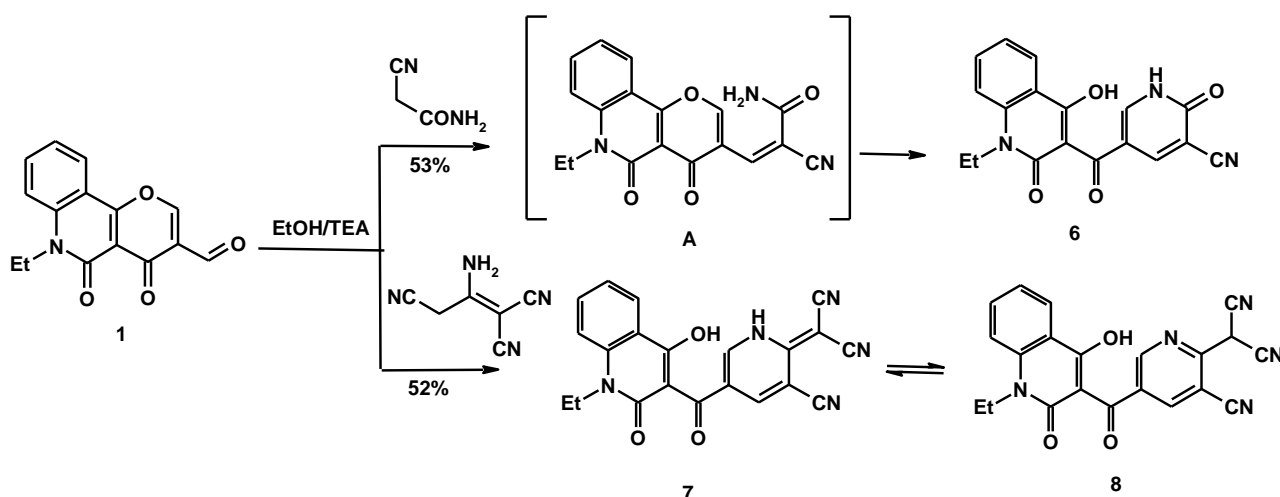
Similarly, carboxaldehyde **1** was reacted with malonic acid, in boiling pyridine, to afford acrylic acid derivative **3** (Scheme 1).¹⁸ The IR spectrum of compound **3** revealed absorption bands at 3446 and 1716 cm^{-1} due to ($O-H$) and ($C=O_{\text{acid}}$) functions. The ^1H NMR spectrum of compound **3** exhibited two characteristic doublets with the same coupling constant ($J=16.5\text{ Hz}$) at δ 6.38 and 6.97, confirming the *E*-configuration around the double bond. In addition, a singlet signal was observed, at δ 8.53, distinguishing the proton appeared at position-2 of γ -pyrone moiety. The mass spectrum of compound **3** showed the molecular ion peak at m/z 311 which agrees with the formula weight (311.29).

The reactivity of aldehyde **1** towards malononitrile was studied under different reaction conditions, such as triethylamine (TEA) in boiling ethanol, boiling in glacial acetic acid, and boiling in distilled water

without any organic solvent or catalyst (green reaction). The condensation process took place when the reaction was carried out in hot distilled water,¹⁹ leading to malononitrile derivative **4**, in 71% yield (Scheme 1). The mass spectrum of compound **4** showed the molecular ion peak at m/z 317 which is in good agreement with its molecular weight. The IR spectrum of compound **4** exhibited characteristic absorption bands at 2224, 1668, and 1637 cm^{-1} assigned to $\text{C}\equiv\text{N}$, $\text{C}=\text{O}_{\gamma\text{-pyrone}}$, and $\text{C}=\text{O}_{\text{quinolone}}$ functional groups, respectively.

Treatment of aldehyde **1** with ethyl cyanoacetate in dry pyridine at room temperature gave cyanoacrylate ester **5** (Scheme 1). The IR spectrum of compound **5** showed characteristic absorption bands at 2212 and 1719 cm^{-1} assigned to the $\text{C}\equiv\text{N}$ and $\text{C}=\text{O}_{\text{ester}}$, respectively. The ^1H NMR spectrum of compound **5** presented two characteristic singlets at δ 7.49 and 8.70 attributed to CH_{vinyl} and H-2 of γ -pyrone, respectively.

Condensation of aldehyde **1** with cyanoacetamide, in boiling ethanol containing few drops of TEA, yielded pyridyl quinolyl ketone **6**.²⁰ As shown in Scheme 2, the reaction may occur initially *via* condensation process (intermediate **A**) followed by nucleophilic attack of amidic nitrogen at C-2 position with concomitant γ -pyrone ring-opening. The IR spectrum of compound **6** displayed characteristic absorption bands at 2211, 1678, and 1636 cm^{-1} , attributed to $\text{C}\equiv\text{N}$, $\text{C}=\text{O}_{\text{pyridone}}$, and $\text{C}=\text{O}_{\text{quinolone}}$, respectively. The ^1H NMR spectrum of compound **6** revealed two singlet signals, at δ 8.26 and 8.38, distinguishing both H-6 and H-4 of pyridine nucleus. The ^{13}C NMR spectrum of compound **6** showed typical signals at δ 116.3, 162.9, 165.5 and 187.2 ppm attributed to $\text{C}\equiv\text{N}$ and $\text{C}=\text{O}_{\text{quinolone}}$, $\text{C}=\text{O}_{\text{pyridone}}$, $\text{C}=\text{O}_{\text{ketone}}$, respectively.



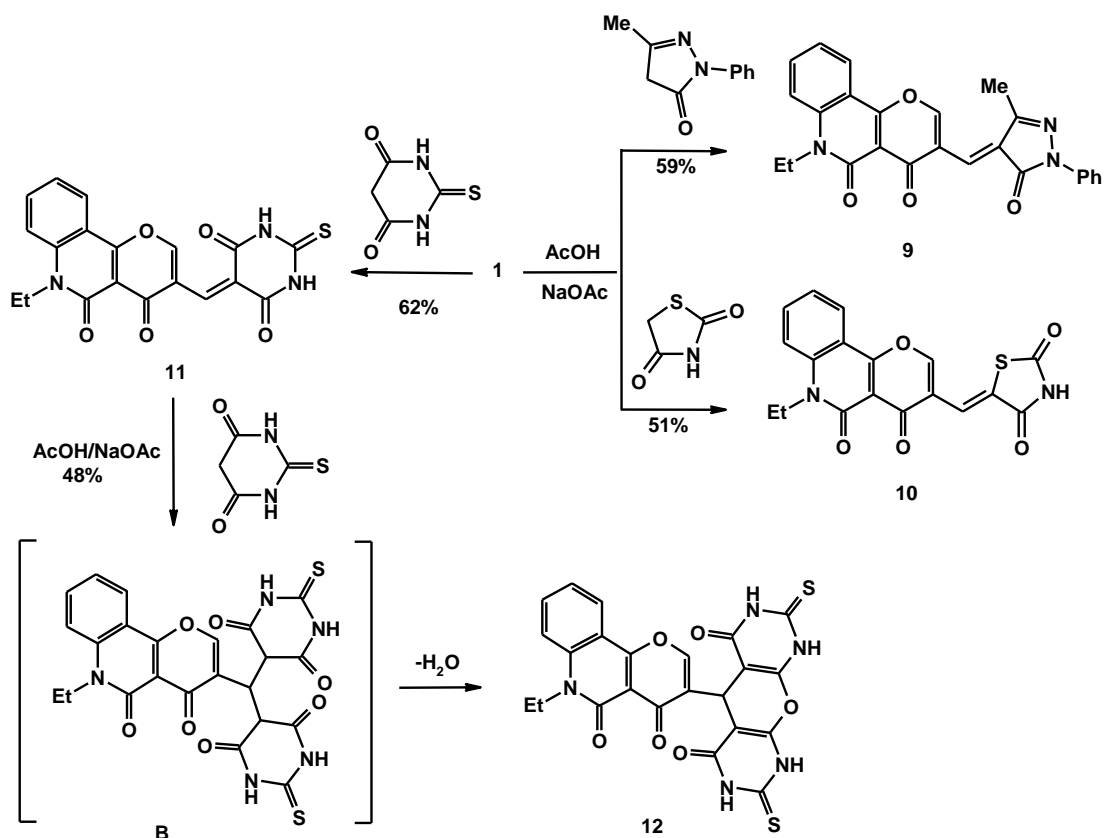
Scheme 2. Condensation of aldehyde **1** with cyanoacetamide and malononitrile dimer

Condensation of aldehyde **1** with malononitrile dimer, in absolute ethanol containing few drops of TEA, led to another multi-substituted pyridyl quinolyl ketone **8** (Scheme 2). IR spectrum of compound **7** showed characteristic absorption bands at 2205 ($\text{C}\equiv\text{N}$), 1644 ($\text{C}=\text{O}_{\text{quinolone}}$) and 1609 cm^{-1} ($\text{C}=\text{O}_{\text{ketone}}$).

Interestingly, the product might exist in two tautomeric forms; 2-pyridylidenemalononitrile **7** and 2-pyridinylmalononitrile **8** (Scheme 2). This transannular imine-enamine like tautomerism was deduced from ^1H NMR spectrum study. ^1H NMR spectrum revealed three characteristic singlet signals, at δ 6.69, 8.34 and 8.89, attributed to protons of $(\text{CH}(\text{CN})_2)$, $(\text{H-2}_{\text{pyridine}})$, and $(\text{H-4}_{\text{pyridine}})$, respectively.

The reactivity of aldehyde **1** towards a variety of cyclic active methylene compounds was studied. Consequently, aldehyde **1** was treated with 3-methyl-1-phenyl-2-pyrazolin-5-one and 1,3-thiazolidine-2,4-dione, in glacial acetic acid containing freshly fused sodium acetate, producing the corresponding methylenepyrazolinone derivative **9** and methylenythiazolidene derivative **10**, respectively (Scheme 3). The IR spectrum of compound **9** showed characteristic absorption bands at 1669 ($\text{C}=\text{O}_{\text{pyrazolone}}$) and 1654 cm^{-1} ($\text{C}=\text{O}_{\gamma\text{-pyrone}}$ and $\text{C}=\text{O}_{\text{quinolone}}$). ^1H NMR spectrum of compound **9** showed two characteristic singlet signals, at δ 6.96 and 8.29, assigned to H_{vinyl} and H-2 of γ -pyrone, respectively. While, the IR spectrum of compound **10** exhibited characteristic absorption bands at 1733, 1684, 1647 and 1636 cm^{-1} assigned to the $(2\text{C}=\text{O}_{\text{thiazolidenedione}})$, $(\text{C}=\text{O}_{\gamma\text{-pyrone}})$ and $(\text{C}=\text{O}_{\text{quinolone}})$, respectively. ^1H NMR spectrum of compound **10** showed two characteristic chemical shifts at δ 7.49 and 8.66, due to CH_{vinyl} and H-2 of γ -pyrone, respectively.

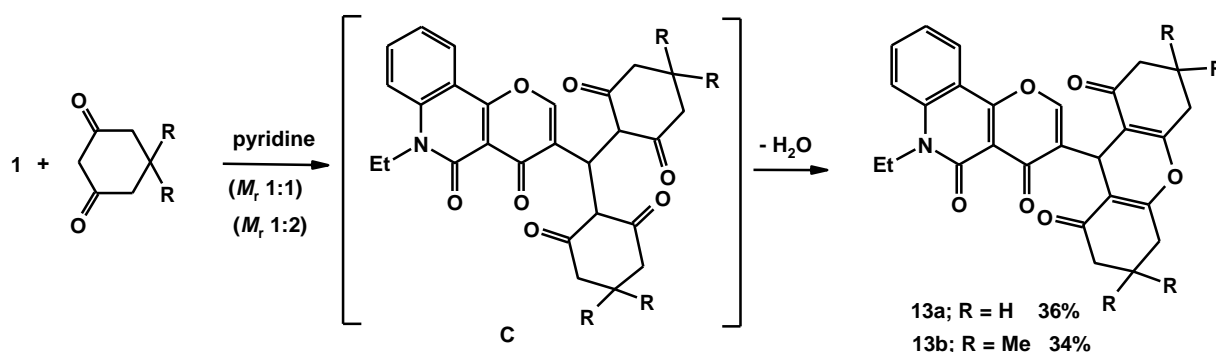
Likewise, condensation of aldehyde **1** with thiobarbituric acid in glacial acetic acid afforded the condensation product **11** (Scheme 3). ^1H NMR spectrum of compound **11** showed two characteristic singlet signals, at δ 5.85 and 8.61, due to H_{vinyl} and H-2 of γ -pyrone, respectively.



Scheme 3. Condensation of aldehyde **1** with some cyclic active methylene compounds

When the latter reaction of aldehyde **1** was carried out using excess amount of thiobarbituric acid (at molar ratio 1:2), dipyrimido[*b,e*]pyran derivative **12** was provided (Scheme 3). This reaction may take place initially *via* condensation between aldehyde **1** and one molecule of thiobarbituric acid producing compound **11** which added another molecule of thiobarbituric acid at the exocyclic vinyl bond (intermediate **B**) with subsequent dehydration. The ^1H NMR spectrum of compound **12** displayed characteristic singlet signals at δ 3.89 (H-4_{pyran}) and 8.11 (H-2 _{γ} -pyrone).

On the other hand, reaction of aldehyde **1** with cyclohexane-1,3-dione and/or dimedone, at molar ratios (1:1 and 1:2) in boiling pyridine, gave xanthenedione derivatives **13a** (R = H) and **13b** (R = Me); *via* the non-isolable intermediate **C** (Scheme 4). The ^1H NMR spectrum of compound **13a** showed characteristic singlet chemical shifts, at δ 3.90 and 8.26, attributable to (H-9_{xanthene}) and (H-2 _{γ} -pyrone), respectively. However, these two specific signals appeared at δ 3.89 and 8.20 for compound **13b**.

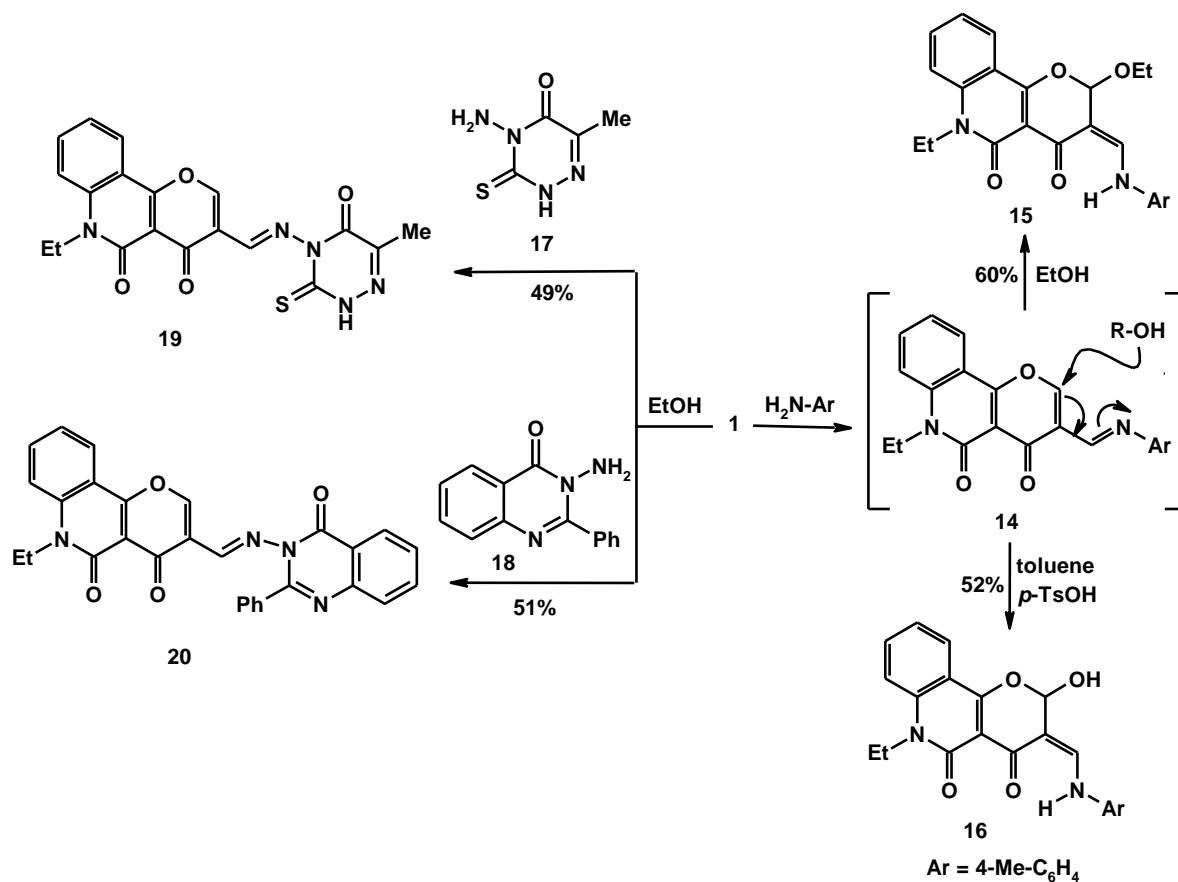


Scheme 4. Condensation of aldehyde **1** with 1,3-cyclohexanediones

Reaction of aldehyde **1** with *p*-toluidine, in the presence of *p*-toluenesulfonic acid in dry toluene, gave 2-hydroxy-3-(aminomethylenyl)pyranoquinoline **15** (Scheme 5). Establishment of structure **15** can be interpreted *via* first formation of the corresponding non isolable azomethine intermediate **14**, which *in situ* undergoes 1,4-addition of a water molecule.²¹ The ^1H NMR spectrum of compound **15** showed characteristic signal, at δ 5.91, due to α -proton of hydroxypyrene (O-CH-OH), and characteristic doublet signal, at δ 8.48, due to an enamine proton (C=CH-NH). The spectrum also revealed two deuterium exchangeable protons at δ 4.80 and 9.35, due to O-H and N-H, respectively.

Interestingly, when the latter reaction was carried out using boiling ethanol instead of toluene without catalyst, another 1,4-adduct; 2-ethoxy-3-(aminomethylenyl)pyranoquinoline derivative **16** was obtained (Scheme 5). The ^1H NMR spectrum of adduct **16** showed distinguishable singlet signal, at δ 5.87, due to α -proton of ethoxypyrene (O-CH-OC₂H₅) at position 2, in addition to two doublets, at δ 7.93 ($J=11.7$) and 11.30 ($J=11.7$ Hz), assigned to an olefinic and NH protons, respectively. The ^{13}C NMR spectrum of

compound **16** showed characteristic signals at δ 15.5 and 61.8 (ethoxycarbonyl carbons), 24.6 (CH_3 arom.) and 146.6 ($\text{CH}_{\text{exocyclic}}$).

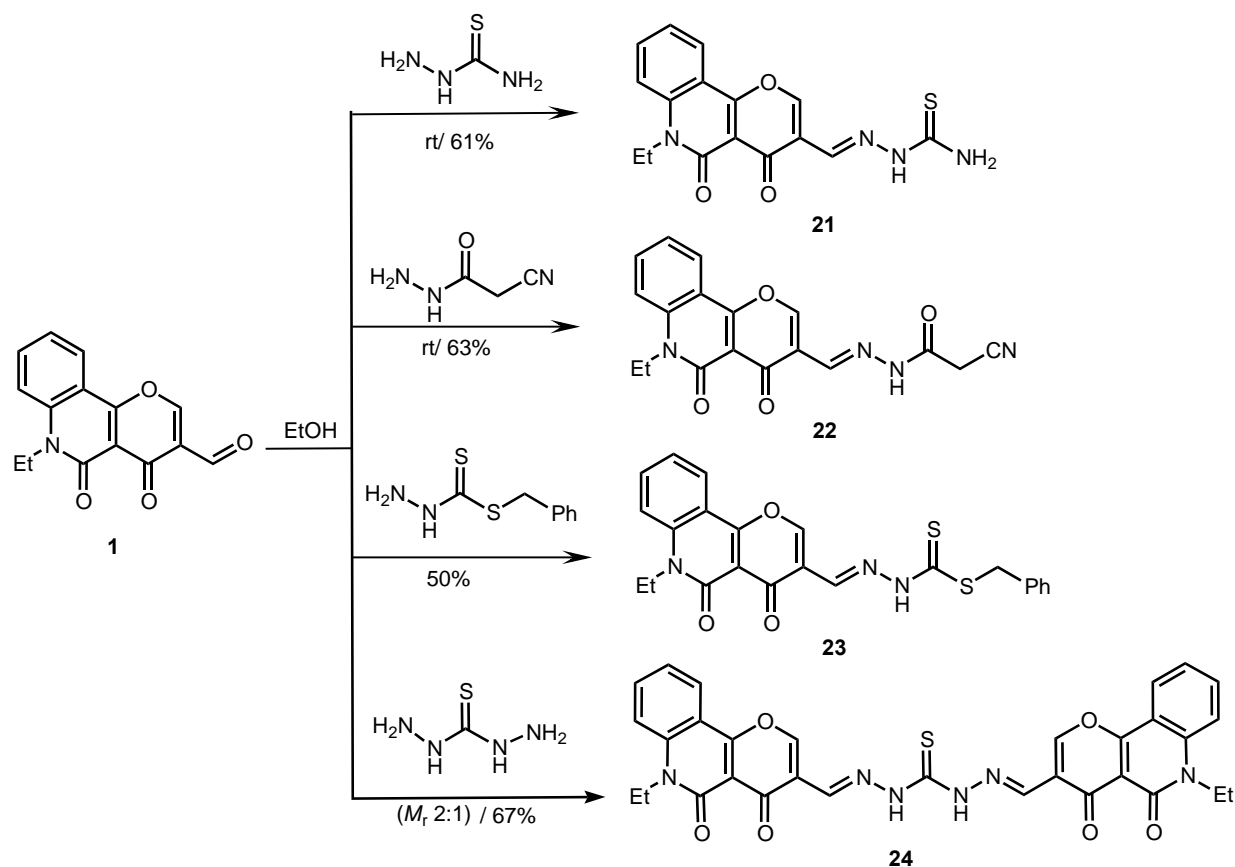


Scheme 5. Reaction of aldehyde **1** with some aryl/hetary amines

Also, condensation of aldehyde **1** with some heterocyclic amines, namely; 4-amino-1,2,4-triazine²² and 3-aminoquinazolinone,²³ was performed in absolute ethanol, affording the corresponding azomethine derivatives **19** and **20** (Scheme 5). The IR spectrum of compound **19** showed characteristic absorption bands, at 1672, 1648 and 1636 cm^{-1} , assigned to $\text{C}=\text{O}_{\text{triazine}}$, $\text{C}=\text{O}_{\gamma\text{-pyrone}}$, and $\text{C}=\text{O}_{\text{quinolone}}$, respectively. The ^1H NMR spectrum of compound **19** presented characteristic singlet signals, at δ 8.65 and 8.73, attributed to $\text{H}_{\text{azomethine}}$ and $\text{H-2}_{\gamma\text{-pyrone}}$, respectively. Also, the spectrum revealed characteristic singlet at δ 2.17 assigned to the methyl protons of the triazine nucleus. The ^{13}C NMR spectrum of compound **19** showed distinctive signals at δ 16.9 (CH_3 triazine), 168.9 ($\text{C}=\text{O}_{\text{triazine}}$), 177.1 ($\text{C}=\text{O}_{\gamma\text{-pyrone}}$) and 183.4 ($\text{C}=\text{S}_{\text{triazine}}$). While, the IR spectrum of compound **20** revealed typical absorption bands, at 1679, 1665 and 1630 cm^{-1} , assigned to $\text{C}=\text{O}_{\text{quinazoline}}$, $\text{C}=\text{O}_{\gamma\text{-pyrone}}$ and $\text{C}=\text{O}_{\text{quinolone}}$ respectively. The ^1H NMR spectrum of compound **20** displayed characteristic singlet signals, at δ 8.60 and 9.13, attributed to protons of $\text{H}_{\text{azomethine}}$ and $\text{H-2}_{\gamma\text{-pyrone}}$, respectively.

Next, the chemical behavior of aldehyde **1** was studied towards some hydrazide derivatives. Reaction of aldehyde **1** with thiosemicarbazide was performed in ethanol at room temperature to give the

corresponding hydrazone **21** (Scheme 6). The characterization of thiosemicarbazone **21** was based on IR spectrum which revealed the presence of absorption bands, at 3416, 3273, 3158 (NH₂, N–H), 1677 (C=O_γ-pyrone), 1642 (C=O_{quinolone}), and 1287 cm⁻¹ (C=S). ¹H NMR spectrum of compound **21** showed characteristic singlet signals, at δ 7.97 and 8.97, due to protons of CH_{azomethine} and H-2_γ-pyrone, respectively.



Scheme 6. Condensation of aldehyde **1** with some hydrazides

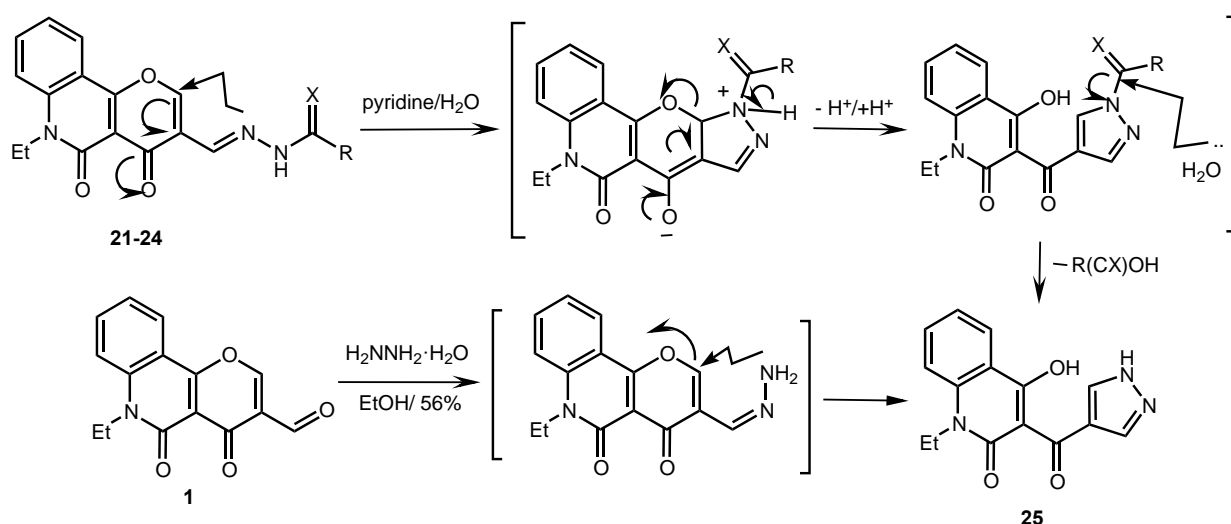
Likewise, condensation of aldehyde **1** with cyanoacetohydrazide and benzyl hydrazinecarbodithioate gave the corresponding hydrazones **22** and **23** (Scheme 6). The IR spectrum of hydrazone **22** revealed an absorption band at 2230 cm⁻¹ (C≡N). The mass spectrum of compound **23** exhibited the molecular ion peak at *m/z* 449 (16%), corresponding to the molecular formula mass. The ¹H NMR spectrum of compound **23** showed characteristic singlet signals, at chemical shifts δ 8.40 and 9.23, due to CH_{azomethine} and H-2_γ-pyrone, respectively.

Treatment of aldehyde **1** with thiocarbonyl dihydrazide, at molar ratio (2:1), in boiling ethanol, resulted in bis-hydrazone derivative **24**, in 67% yield (Scheme 6). The mass spectrum of compound **24** presented the molecular ion peak at *m/z* 608, corresponding to the molecular formula (C₃₁H₂₄N₆O₆S).

It was found that boiling any of hydrazone derivatives **21-24** in aqueous pyridine led to the same new product; pyrazolyl quinolyl ketone **25**. As depicted in Scheme 7, an intramolecular nucleophilic attack can take place between nitrogen of the hydrazone side chain (nucleophile) and the position 2 of pyrone

ring (an electron deficient center), effecting ring-opening/ring-closure, completed by hydrolysis of pyrazole *N*-substituent.²⁴ Structure of pyrazole **25** was deduced from its analytical and spectral data. Thus, elemental analysis of these compounds revealed absence of sulfur and showed good accordance with calculated percentages for C, H, and N elements ($\pm 0.4\%$). Mass spectrum presented the molecular ion peak, at m/z 283, which agreed well with the molecular formula mass (283.28). The IR spectrum presented characteristic vibrational absorption bands, at $\tilde{\nu}$ 3420 (O–H), 3143 (N–H), 1646 and 1624 cm^{-1} ($2\text{C}=\text{O}$). ^1H NMR spectrum of pyrazole **25** showed two singlet signals at, δ 8.14 and 8.38, assigned to pyrazole ring protons. In addition, the spectrum presented two broad signals, at δ 13.39 and 14.01, due to deuterium exchangeable protons of (NH) and (OH), respectively.

Furthermore, structural elucidation of the product **25** received a good support when the same product (identical in every respect) was prepared by the reaction of aldehyde **1** with hydrazine hydrate, in boiling ethanol (Scheme 7).



Scheme 7. Conversion of aldehyde **1** and hydrazones **21-24** into pyrazole **25**

EXPERIMENTAL

Melting points were determined on a digital Stuart SMP3 apparatus. Infrared spectra were taken on FT-IR Nicolet IS10 spectrophotometer (cm^{-1}), using KBr disks. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were measured on Mercury-300BB, using $\text{DMSO}-d_6$ as a solvent and tetramethylsilane as an internal standard. Mass spectra were measured using GC-2010 Shimadzu Gas chromatography instrument mass spectrometer (70 eV) GC-MS qp 1000 ex Shimadzu instrument (70 eV). Elemental microanalyses were performed on a Perkin-Elmer CHN-2400 analyzer at the Chemical War Department, Ministry of Defense, Egypt. 6-Ethyl-4,5-dioxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinoline-3-carboxaldehyde (**1**) was prepared according to literature method.¹⁶

(2*E*)-3-(6-Ethyl-5,6-dihydro-4,5-dioxo-4*H*-pyrano[3,2-*c*]quinolin-3-yl)prop-2-enitrile (**2**). A

mixture of aldehyde **1** (0.54 g, 2 mmol) and cyanoacetic acid (0.17 g, 2 mmol) in pyridine (20 mL) was heated under reflux for 1 h. After cooling at room temperature, the reaction mixture was poured onto crushed ice and neutralized with concentrated HCl. The precipitate so formed was filtered and crystallized from EtOH to give compound **2** as yellow crystals, yield (0.31 g, 53%), mp 176-177 °C. IR (KBr, cm^{-1}): 3073 ($\text{CH}_{\text{arom.}}$), 2976, 2931 ($\text{CH}_{\text{aliph.}}$), 2204 ($\text{C}\equiv\text{N}$), 1666 ($\text{C}=\text{O}_{\gamma\text{-pyrone}}$), 1636 ($\text{C}=\text{O}_{\text{quinolone}}$) and 1611 ($\text{C}=\text{C}$). ^1H NMR ($\text{DMSO-}d_6$, δ , 300 MHz): 1.13 (t, 3H, CH_2CH_3), 4.10 (q, 2H, CH_2CH_3), 7.34 (t, 1H, $J=7.5$ Hz, H-9), 7.52-7.82 (m, 2H, H-7 and H-8), 8.06 (d, 1H, H-10), 8.44 (s, 1H, H-2), 8.68 (d, 1H, $J=13.8$ Hz, $\text{CH}_{\text{olefinic}}$) and 9.07 (d, 1H, $J=13.8$ Hz, $\text{CH}_{\text{olefinic}}$). ^{13}C NMR ($\text{DMSO-}d_6$, δ , 75 MHz): 12.4, 37.6, 91.3, 105.5, 115.2, 116.8, 121.9, 123.7, 124.5, 126.1, 128.3, 134.7, 148.4, 162.6, 167.8, 173.2, 178.6. Mass spectrum, m/z (I_r %): 292 (M^+ , 26), 209 (22), 189 (22), 184 (100), 170 (30), 143 (26), 132 (30), 116 (35), 91 (43), 77 (52) and 65 (48). Anal. Calcd for $\text{C}_{17}\text{H}_{12}\text{N}_2\text{O}_3$ (292.29); C, 69.86; H, 4.14; N, 9.58%. Found: C, 69.72; H, 4.11; N, 9.53%.

(2E)-3-(6-Ethyl-5,6-dihydro-4,5-dioxo-4H-pyrano[3,2-c]quinolin-3-yl)prop-2-enoic acid (3).

A mixture of aldehyde **1** (0.54 g, 2 mmol) and malonic acid (0.21 g, 2 mmol) in pyridine (20 mL) was heated under reflux for 1 h. After cooling at room temperature, the reaction mixture was poured onto crushed ice and neutralized with concentrated HCl. The precipitate so formed was filtered and crystallized from AcOH to give compound **3** as yellow crystals, yield (0.42 g, 68%), mp 181-182 °C. IR (KBr, cm^{-1}): 3446 (OH), 3079 ($\text{CH}_{\text{arom.}}$), 2973, 2935 ($\text{CH}_{\text{aliph.}}$), 1716 ($\text{C}=\text{O}_{\text{acid}}$), 1636 ($\text{C}=\text{O}_{\gamma\text{-pyrone}}$ and $\text{C}=\text{O}_{\text{quinolone}}$) and 1616 ($\text{C}=\text{C}$). ^1H NMR ($\text{DMSO-}d_6$, δ , 300 MHz): 1.21 (t, 3H, $J=6.6$ Hz, CH_2CH_3), 4.34 (q, 2H, $J=6.6$ Hz, CH_2CH_3), 6.38 (d, 1H, $J=16.5$ Hz, $\text{CH}_{\text{olefinic}}$), 6.97 (d, 1H, $J=16.5$ Hz, $\text{CH}_{\text{olefinic}}$), 7.15-7.81 (m, 3H, Ar-H), 8.09 (d, 1H, H-10), 8.53 (s, 1H, H-2) and 12.29 (bs, 1H, COOH exchangeable with D_2O). ^{13}C NMR ($\text{DMSO-}d_6$, δ , 75 MHz): 12.6, 37.5, 105.8, 115.3, 117.7, 121.6, 123.7, 124.9, 126.2, 128.6, 135.3, 145.8, 152.6, 162.4, 168.0, 172.6, 178.2. Mass spectrum, m/z (I_r %): 311 (M^+ , 31), 267 (27), 241 (40), 213 (31), 200 (24), 188 (44), 172 (16), 161 (34), 159 (11), 145 (20), 132 (64), 116 (33), 119 (31), 104 (56), 91 (51), 77 (100) and 64 (14). Anal. Calcd for $\text{C}_{17}\text{H}_{13}\text{NO}_5$ (311.29); C, 65.59; H, 4.21; N, 4.50%. Found: C, 65.43; H, 4.23; N, 4.38%.

2-[(6-Ethyl-5,6-dihydro-4,5-dioxo-4H-pyrano[3,2-c]quinolin-3-yl)methylene]malononitrile (4). To a suspension of aldehyde **1** (0.54 g, 2 mmol) in distilled water (20 mL), malononitrile (0.13 g, 2 mmol) in distilled water (5 mL) was added and the reaction mixture was heated under reflux for 15 min. The solid so formed was filtered while hot and crystallized from EtOH to give compound **4** as yellow crystals, yield (0.45 g, 71%), mp 246-247 °C. IR (KBr, cm^{-1}): 2977, 2937 ($\text{CH}_{\text{aliph.}}$), 2224 ($\text{C}\equiv\text{N}$), 1668 ($\text{C}=\text{O}_{\gamma\text{-pyrone}}$), 1637 ($\text{C}=\text{O}_{\text{quinolone}}$) and 1614 ($\text{C}=\text{C}$). ^1H NMR ($\text{DMSO-}d_6$, δ , 300 MHz): 1.16 (t, 3H, $J=6.6$ Hz, CH_2CH_3), 4.21 (q, 2H, $J=6.6$ Hz, CH_2CH_3), 7.22 (t, 1H, $J=6.9$ Hz, H-9), 7.46 (d, 1H, $J=8.7$ Hz, H-7), 7.67 (t, 1H, $J=8.7$ Hz, H-8), 8.09 (d, 1H, $J=8.4$ Hz, H-10), 8.15 (s, 1H, CH_{vinyl}) and 8.20 (s, 1H, H-2). Mass spectrum,

m/z (I_r %): 317 (M^+ , 8), 260 (5), 210 (6), 173 (11), 160 (6), 132 (9), 119 (11), 117(10), 91 (22), 77 (19), 64 (25) and 55 (100). Anal. Calcd for $C_{18}H_{11}N_3O_3$ (317.30); C, 68.14; H, 3.49; N, 13.24%. Found: C, 67.96; H, 3.25; N, 13.11%.

Ethyl 2-cyano-3-(6-ethyl-5,6-dihydro-4,5-dioxo-4H-pyrano[3,2-c]quinolin-3-yl)acrylate (5). A mixture of aldehyde **1** (0.54 g, 2 mmol) and ethyl cyanoacetate (0.23 g, 2 mmol) in pyridine (20 mL) was stirred at room temperature for 2 h. The reaction mixture was poured onto crushed ice and neutralized with concentrated HCl. The solid obtained was filtered and crystallized from EtOH to give compound **5** as yellow crystals, (0.50 g, 68%), mp 180-181 °C. IR (KBr, cm^{-1}): 2979, 2934 ($CH_{aliph.}$), 2212 ($C\equiv N$), 1719 ($OC=O$), 1644 ($C=O_{\gamma\text{-pyrone}}$ and $C=O_{quinolone}$) and 1616 ($C=C$). 1H NMR (DMSO- d_6 , δ , 300 MHz): 1.21-1.35 (m, 6H, CH_2CH_3), 4.23-4.38 (m, 4H, $2CH_2CH_3$), 7.38 (t, 1H, $J=8.4$ Hz, H-9), 7.49 (s, 1H, CH_{vinyl}), 7.68 (d, 1H, $J=7.5$ Hz, H-7), 7.86 (t, 1H, $J=7.2$ Hz, H-8), 8.11 (d, 1H, $J=7.2$ Hz, H-10) and 8.70 (s, 1H, H-2). Mass spectrum, m/z (I_r %): 363 (M^+-1 , 13), 292 (7), 266 (24), 241 (71), 213 (29), 185 (51), 145 (11), 132 (31), 119 (31), 91 (20), 77 (73), 64 (42) and 57(100). Anal. Calcd for $C_{20}H_{16}N_2O_5$ (364.36); C, 65.93; H, 4.43; N, 7.69%. Found: C, 65.74; H, 4.35; N, 7.54%.

3-[(3-Cyano-1,2-dihydro-2-oxopyridin-5-yl)carbonyl]-1-ethyl-4-hydroxyquinolin-2(1H)-one (6). A mixture of aldehyde **1** (0.54 g, 2 mmol) and cyanoacetamide (0.17 g, 2 mmol) in absolute EtOH containing few drops of TEA was heated under reflux for 1 h. After cooling at room temperature, the precipitate so formed was filtered and crystallized from DMF to give compound **6** as yellow crystals, yield (0.38 g, 53%), mp > 300 °C. IR (KBr, cm^{-1}): 3421 (OH, NH), 2975, 2955 ($CH_{aliph.}$), 2211 ($C\equiv N$), 1678 ($C=O_{pyridone}$), 1636 ($C=O_{quinolone}$), 1625 ($C=O_{hydrogen\ bonded}$) and 1605 ($C=C$). 1H NMR (DMSO- d_6 , δ , 300 MHz): 1.27 (t, 3H, $J=7.8$ Hz, CH_2CH_3), 4.27 (q, 2H, $J=7.8$, CH_2CH_3), 7.46 (t, 1H, $J=7.5$ Hz, H-6_{quinoline}), 7.78 (d, $J=9$ Hz, 1H, H-8_{quinoline}), 7.85 (t, 1H, $J=6.9$, H-7_{quinoline}), 8.11 (d, 1H, $J=6.9$ Hz, H-5_{quinoline}), 8.26 (s, 1H, H-4_{pyridine}), 8.38 (s, 1H, H-6_{pyridine}), 12.79 (bs, 1H, NH exchangeable with D_2O) and 12.89 (bs, 1H, OH exchangeable with D_2O). ^{13}C NMR (DMSO- d_6 , δ , 75 MHz): 12.5, 38.1, 101.6, 104.3, 115.2, 116.3, 122.2, 124.1, 125.9, 128.7, 130.1, 134.9, 138.5, 147.2, 159.4, 162.9, 165.5, 187.2. Mass spectrum, m/z (I_r %): 308 (M^+-27 , 9), 279 (1), 215 (4), 188(3), 145 (1), 132 (4), 119 (2), 110 (100), 91 (2), 77 (10) and 64 (2). Anal. Calcd for $C_{18}H_{13}N_3O_4$ (335.32); C, 64.47; H, 3.91; N, 12.53%. Found: C, 64.25; H, 3.82; N, 12.51%.

{3-Cyano-5-[(1-ethyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)carbonyl]pyridin-2(1H)-ylidene}propanedinitrile (7) and {3-cyano-5-[(1-ethyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)carbonyl]pyridin-2-yl}propanedinitrile (8). A mixture of aldehyde **1** (0.54 g, 2 mmol) and 2-aminoprop-1-ene-1,1,3-tricarbonitrile (0.26 g, 2 mmol) in absolute EtOH containing drops of TEA was heated under reflux for 1 h. After cooling at room temperature, the precipitate so formed was filtered and crystallized from EtOH to give compounds **7** and **8** as yellow crystals, yield (0.40 g, 52%), mp 230-231

°C. IR (KBr, cm^{-1}): 3425 (OH, NH), 2977, 2937 ($\text{CH}_{\text{aliph.}}$), 2205 ($\text{C}\equiv\text{N}$), 1644 ($\text{C}=\text{O}_{\text{quinolone}}$ and $\text{C}=\text{O}_{\text{hydrogen bonded}}$), 1609 ($\text{C}=\text{N}$) and 1577 ($\text{C}=\text{C}$). ^1H NMR ($\text{DMSO}-d_6$, δ , 300 MHz): 1.22 (t, 3H, $J=7.2$ Hz, CH_2CH_3), 4.28 (q, 2H, $J=7.2$, CH_2CH_3), 6.69 (s, 1H, $\text{CH}(\text{CN})_2$), 7.34 (t, 1H, $J=7.8$ Hz, Ar-H), 7.55 (d, 1H, $J=8.7$ Hz, Ar-H), 7.75 (t, 1H, $J=8.7$, Ar-H), 8.11 (d, 1H, $J=7.8$ Hz, Ar-H), 8.34 (s, 1H, H-2_{pyridine}), 8.47 (bs, NH exchangeable with D_2O) and 8.89 (s, 1H, H-4_{pyridine}). Mass spectrum, m/z (I_r %): 384 ($\text{M}^+ + 1$, 52), 383 (M^+ , 88), 358 (63), 304 (61), 293 (100), 216 (62), 188 (60), 157 (52), 132 (75), 89 (66) and 79 (69). Anal. Calcd for $\text{C}_{21}\text{H}_{13}\text{N}_5\text{O}_3$ (383.36); C, 65.79; H, 3.42; N, 18.27%. Found: C, 65.58; H, 3.31; N, 18.10%.

Reaction of aldehyde 1 with some active methylene compounds. General procedure for synthesis of compounds 9–11. A mixture of aldehyde 1 (0.54 g, 2 mmol) and some active methylene nucleophiles namely; 3-methyl-1-phenyl-2-pyrazolin-5-one, 1,3-thiazolidine-2,4-dione and thiobarbituric acid (2 mmol), in glacial acetic acid (10 mL) containing freshly fused sodium acetate (0.1 g), was heated under reflux for 2 h. The solid deposited after cooling was filtered and crystallized from the proper solvent to give the corresponding condensates 9–11, respectively.

6-Ethyl-3-[(3-methyl-1-phenyl-5-oxo-1,5-dihydro-4H-pyrazol-4-ylidene)methyl]-4H-pyrano[3,2-c]-quinoline-4,5(6H)-dione (9). This compound was crystallized from AcOH as yellow crystals, yield (0.50 g, 59%), mp 265–266 °C. IR (KBr, cm^{-1}): 3014 ($\text{CH}_{\text{arom.}}$), 2938, 2856 ($\text{CH}_{\text{aliph.}}$), 1669 ($\text{C}=\text{O}_{\text{pyrazolone}}$), 1654 ($\text{C}=\text{O}_{\gamma\text{-pyrone}}$, $\text{C}=\text{O}_{\text{quinolone}}$), 1617 ($\text{C}=\text{N}$) and 1594 ($\text{C}=\text{C}$). ^1H NMR ($\text{DMSO}-d_6$, δ , 300 MHz): 1.22 (t, 3H, $J=6.9$ Hz, CH_2CH_3), 2.38 (s, 3H, CH_3 pyrazolone), 4.26 (q, 2H, $J=6.9$ Hz, CH_2CH_3), 6.96 (s, 1H, CH_{vinyl}), 7.33–7.78 (m, 7H, Ar-H), 7.86 (d, 1H, $J=7.8$ Hz, H-8), 8.11 (d, 1H, H-10) and 8.29 (s, 1H, H-2). Mass spectrum, m/z (I_r %): 425 (M^+ , 3), 410 (1), 358 (82), 355 (1), 216 (2), 210 (4), 188 (4), 185 (10), 161 (4), 157 (2), 132 (10), 119 (8), 91 (47), 77 (100) and 64 (61). Anal. Calcd for $\text{C}_{25}\text{H}_{19}\text{N}_3\text{O}_4$ (425.45); C, 70.58; H, 4.50; N, 9.88%. Found: C, 70.51; H, 4.43; N, 9.68%.

3-[(2,4-Dioxo-1,3-thiazolidin-5-ylidene)methyl]-6-ethyl-4H-pyrano[3,2-c]quinoline-4,5(6H)-dione (10). This compound was crystallized from AcOH as yellow crystals, yield (0.48 g, 51%), mp 175–176 °C. IR (KBr, cm^{-1}): 3446 (NH), 2976, 2934 ($\text{CH}_{\text{aliph.}}$), 1733, 1684 ($2\text{C}=\text{O}_{\text{thiazolidinedione}}$), 1647 ($\text{C}=\text{O}_{\gamma\text{-pyrone}}$), 1636 ($\text{C}=\text{O}_{\text{quinolone}}$) and 1559 ($\text{C}=\text{C}$). ^1H NMR ($\text{DMSO}-d_6$, δ , 300 MHz): 1.06 (t, 3H, $J=7.5$ Hz, CH_2CH_3), 4.28 (q, 2H, $J=7.5$ Hz, CH_2CH_3), 7.42 (t, 1H, H-7), 7.49 (s, 1H, CH_{vinyl}), 7.69 (d, 1H, H-9), 7.80 (t, 1H, H-8), 8.18 (d, 1H, $J=6.3$ Hz, H-10) and 8.66 (s, 1H, H-2). ^{13}C NMR ($\text{DMSO}-d_6$, δ , 75 MHz): 12.5, 38.1, 101.6, 104.3, 115.2, 119.5, 122.2, 124.1, 125.9, 128.7, 130.1, 134.9, 138.5, 147.2, 159.4, 162.9, 165.5, 187.2. Mass spectrum, m/z (I_r %): 367 ($\text{M}^+ - 1$, 3), 189 (65), 172 (26), 161 (44), 132 (100), 119 (56), 91 (44), 77 (88) and 64 (53). Anal. Calcd for $\text{C}_{18}\text{H}_{12}\text{N}_2\text{O}_5\text{S}$ (368.37); C, 58.69; H, 3.28; N, 7.60; S, 8.70%. Found: C, 58.55; H, 3.17; N, 7.49; S, 8.45%.

3-[(4,6-Dioxo-2-thioxotetrahydropyrimidin-5(2H)-ylidene)methyl]-6-ethyl-4H-pyrano[3,2-c]-

quinoline-4,5(6H)-dione (11). This compound was crystallized from DMF/H₂O as yellow crystals, yield (0.49 g, 62%), mp 270-271 °C. IR (KBr, cm⁻¹): 3425 (2NH), 3073 (CH_{arom.}), 2964, 2930, 2850 (CH_{aliph.}), 1676 (2C=O_{pyrimidine} and C=O_{γ-pyrone}), 1623 (C=O_{quinolone}), 1563 (C=C) and 1235 (C=S). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 1.60 (t, 3H, CH₂CH₃), 4.21 (q, 2H, CH₂CH₃), 5.85 (s, 1H, CH_{vinyl}), 7.21 (t, 1H, *J*=7.5 Hz, H-7), 7.50 (d, 1H, *J*=8.1 Hz, H-9), 7.61 (t, 1H, *J*=8.1 Hz, H-9), 7.90 (d, 1H, *J*=7.8 Hz, H-10), 8.61 (s, 1H, H-2), 11.44 (bs, 2H, NH exchangeable with D₂O). ¹³C NMR (DMSO-*d*₆, δ, 75 MHz): 12.6, 38.4, 106.1, 115.7, 121.2, 123.6, 125.1, 126.5, 128.8, 135.0, 146.8, 158.3, 161.2, 164.0, 168.9, 170.4, 172.3, 175.7, 184.1. Anal. Calcd for C₁₉H₁₃N₃O₅S (395.39); C, 57.72; H, 3.31; N, 10.63; S, 8.11%. Found: C, 57.61; H, 3.26; N, 10.49; S, 8.02%.

5-(4,5-Dioxo-6-ethyl-5,6-dihydro-4H-pyrano[3,2-*c*]quinolin-3-yl)-2,8-dithioxo-5,7,8,9-tetrahydro-2H-pyrimido[5',4':5,6]pyrano[2,3-*d*]pyrimidine-4,6(1H,3H)-dione (12). A mixture of aldehyde **1** (0.54 g, 2 mmol) and thiobarbituric acid (0.58 g, 4 mmol) in glacial acetic acid (10 mL) containing freshly fused sodium acetate (0.1 g), was heated under reflux for 2 h. The solid deposited after cooling was filtered and crystallized from DMF to give compound **12** as yellow crystals yield (0.50 g, 48%), mp > 300 °C. IR (KBr, cm⁻¹): 3421 (NH), 2969, 2925 (CH_{aliph.}), 1730 (C=O_{pyrimidone}), 1670 (C=O_{γ-pyrone}), 1624 (C=O_{quinolone}), 1557 (C=C) and 1248 (C=S). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 1.11 (t, 3H, *J*=6.9 Hz, CH₂CH₃), 3.89 (s, 1H, H-4_{pyran}), 4.25 (q, 2H, *J*=6.9 Hz, CH₂CH₃), 7.18-7.74 (m, 3H, Ar-H), 7.94 (d, 1H, *J*=7.8 Hz, H-10), 8.11 (s, 1H, H-2), 11.04 (bs, 2H, 2NH exchangeable with D₂O) and 11.56 (bs, 2H, 2NH exchangeable with D₂O). Anal. Calcd for C₂₃H₁₅N₅O₆S₂ (521.53); C, 52.97; H, 2.90; N, 13.43; S, 12.30%. Found: C, 52.81; H, 2.75; N, 13.21; S, 12.18%.

9-(4,5-Dioxo-6-ethyl-5,6-dihydro-4H-pyrano[3,2-*c*]quinolin-3-yl)-1,2,3,4,5,6,7,8-octahydroxanthene-1,8-dione (13a). A mixture of aldehyde **1** (0.54 g, 2 mmol) and 1,3-cyclohexanedione (0.23 g, 2 mmol) in dry pyridine was stirred at room temperature for 3 h. The solid deposited after precipitation with dilute HCl was filtered and crystallized from AcOH to give compound **13a** as yellow crystals, yield (0.33 g, 36%), mp 230-231 °C. IR (KBr, cm⁻¹): 2934, 2880 (CH_{aliph.}), 1679, 1645 (4 C=O) and 1610 (C=C) cm⁻¹. ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 1.19 (t, 3H, *J*=7.2 Hz, CH₂CH₃), 1.91-1.95 (m, 4H, 2CH₂), 2.27 (t, 4H, *J*=5.7 Hz, 2CH₂), 2.61 (t, 4H, *J*= 5.7 Hz, 2CH₂), 3.90 (s, 1H, H-9_{xanthene}), 4.23 (q, 2H, *J*=7.2 Hz, CH₂CH₃), 7.38 (t, 1H, *J*=7.8 Hz, H-9), 7.62 (d, 1H, *J*=8.7 Hz, H-7), 7.79 (t, 1H, *J*=8.7 Hz, H-8), 8.12 (d, 1H, *J*=8.4 Hz, H-10) and 8.26 (s, 1H, H-2_{γ-pyrone}). ¹³C NMR (DMSO-*d*₆, δ, 75 MHz): 12.4, 19.9, 25.9, 26.5, 36.3, 38.9, 111.3, 112.4, 114.8, 122.2, 123.6, 127.2, 134.0, 135.6, 139.0, 153.0, 157.0, 166.4, 172.5, 196.4. Mass spectrum, *m/z* (*I*_r %): 457 (M⁺, 15), 217 (33), 216 (30), 188 (52), 132 (44), 119 (41), 110 (19), 91 (74), 76 (26), 64 (63) and 55 (100). Anal. Calcd for C₂₇H₂₃NO₆ (457.47); C, 70.89; H, 5.07; N, 3.06%. Found: C, 70.74; H, 5.11; N, 2.97%.

9-(4,5-Dioxo-6-ethyl-5,6-dihydro-4H-pyrano[3,2-*c*]quinolin-3-yl)-3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8-

octahydroxanthene-1,8-dione (13b). A mixture of aldehyde **1** (0.54 g, 2 mmol) and 5,5-dimethylcyclohexanedione (0.28 g, 2 mmol) in dry pyridine was stirred at room temperature for 3 h. The solid deposited after precipitation with dilute HCl was filtered and crystallized from AcOH to give compound **13b** as yellow crystals, yield (0.35 g, 34%), mp 270-271 °C. IR (KBr, cm^{-1}): 2961, 2929 ($\text{CH}_{\text{aliph.}}$), 1670, 1646, 1635 (4 C=O) and 1612 (C=C). ^1H NMR (DMSO- d_6 , δ , 300 MHz): 0.97 (s, 6H, 2 CH_3), 0.99 (s, 6H, 2 CH_3), 1.24 (t, 3H, CH_2CH_3), 2.27 (s, 4H, 2 CH_2), 3.01 (s, 4H, 2 CH_2), 3.89 (s, 1H, H-9 $_{\text{xanthene}}$), 4.24 (q, 2H, CH_2CH_3), 7.20-7.90 (m, 4H, Ar-H) and 8.20 (s, 1H, H-2 $_{\gamma\text{-pyrone}}$). Mass spectrum, m/z (I_{r} %): 513 (M^+ , 19), 485 (22), 400 (16), 273 (78), 217 (37), 189 (44), 173 (19), 145 (19), 161 (59), 132 (66), 119 (41), 91 (34), 77 (78), 64 (22) and 55 (100). Anal. Calcd for $\text{C}_{31}\text{H}_{31}\text{NO}_6$ (513.58); C, 72.50; H, 6.08; N, 2.73%. Found: C, 72.42; H, 6.01; N, 2.51%.

(3Z)-6-Ethyl-2-hydroxy-3-[(4-methylphenyl)amino]methylidene}-2H-pyrano[3,2-c]quinoline-4,5(3H,6H)-dione (15). A mixture of aldehyde **1** (0.54 g, 2 mmol) and *p*-toluidine (0.21 g, 2 mmol) in dry toluene in presence of *p*-toluenesulfonic acid was heated under reflux for 4 h. The solid obtained after cooling was filtered and crystallized from petroleum ether 60-80 to give compound **15** as yellow crystals, yield (0.45 g, 60%), mp > 300 °C. IR (KBr, cm^{-1}): 3420 (OH), 3049 ($\text{CH}_{\text{arom.}}$), 2972, 2928 ($\text{CH}_{\text{aliph.}}$), 1647 (C=O $_{\text{quinolone}}$), 1632 (C=O $_{\text{hydrogen bonded}}$) and 1590 (C=C). ^1H NMR (DMSO- d_6 , δ , 300 MHz): 1.23 (t, 3H, $J=6.9$ Hz, CH_2CH_3), 2.27 (s, 3H, CH_3), 4.21 (q, 2H, $J=6.6$ Hz, CH_2CH_3), 4.80 (bs, 1H, OH exchangeable with D_2O), 5.91 (s, 1H, O-CHO), 6.47 (d, 1H, $J=8.1$ Hz, Ar-H), 7.03-7.53 (m, 4H, Ar-H), 7.91 (d, 1H, Ar-H), 8.06 (d, 1H, $J=6.3$ Hz, Ar-H), 8.48 (d, 1H, $J=11.4$ Hz, $\text{CH}_{\text{olefinic}}$) and 9.35 (d, 1H, $J=11.4$ Hz, NH exchangeable with D_2O). Anal. Calcd for $\text{C}_{22}\text{H}_{20}\text{N}_2\text{O}_4$ (376.41); C, 70.20; H, 5.36; N, 7.44%. Found: C, 70.06; H, 5.14; N, 7.17%.

(3Z)-2-Ethoxy-6-ethyl-3-[(4-methylphenyl)amino]methylidene}-2H-pyrano[3,2-c]quinoline-4,5(3H,6H)-dione (16). A mixture of aldehyde **1** (0.54 g, 2 mmol) and *p*-toluidine (0.21 g, 2 mmol) in absolute EtOH was heated under reflux for 4 h. The solid obtained after cooling was filtered and crystallized from EtOH to give compound **16** as yellow crystals, yield (0.42 g, 52%), mp 184-185 °C. IR (KBr, cm^{-1}): 3421 (NH), 2973, 2934 ($\text{CH}_{\text{aliph.}}$), 1635 (C=O $_{\text{quinolone}}$), 1628 (C=O $_{\text{hydrogen bonded}}$) and 1559 (C=C). ^1H NMR (DMSO- d_6 , δ , 300 MHz): 1.02-1.23 (m, 6H, 2 CH_2CH_3), 2.28 (s, 3H, CH_3), 4.03-4.24 (m, 4H, 2 CH_2CH_3), 5.87 (s, 1H, O-CHO), 6.82-7.71 (m, 7H, Ar-H), 7.93 (d, 1H, $J=11.7$ Hz, $\text{CH}_{\text{olefinic}}$), 8.05 (d, 1H, H-10) and 11.30 (d, 1H, $J=11.7$ Hz, NH exchangeable with D_2O). Mass spectrum, m/z (I_{r} %): 404 (M^+ , 9), 373 (14), 360 (11), 332 (14), 311 (11), 266 (9), 212 (9), 187 (9), 161 (11), 158 (10), 142 (11), 133 (10), 91 (20), 89 (14), 77 (100), and 64 (45). ^{13}C NMR (DMSO- d_6 , δ , 75 MHz): 12.2, 15.5, 24.6, 38.1, 61.8, 76.3, 99.2, 115.6, 117.4, 120.1, 122.3, 124.8, 126.2, 128.3, 130.2, 135.0, 139.2, 146.6, 159.6, 161.5, 164.3, 174.5. Anal. Calcd for $\text{C}_{24}\text{H}_{24}\text{N}_2\text{O}_4$ (404.46); C, 71.27; H, 5.98; N, 6.93%. Found: C, 71.04; H, 5.71; N, 6.85%.

6-Ethyl-3-[(6-methyl-5-oxo-3-thioxo-2,5-dihydro-1,2,4-triazin-4(3*H*)-yl)imino]methyl]-4*H*-pyrano[3,2-*c*]quinoline-4,5(6*H*)-dione (19). A mixture of aldehyde **1** (0.54 g, 2 mmol) and 4-amino-6-methyl-3-thioxo-3,4-dihydro-1,2,4-triazin-5(2*H*)-one (**17**) (0.32 g, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 2 h. The solid obtained after cooling was filtered and crystallized from DMF to give compound **19** as dark yellow crystals, yield (0.40 g, 49%), mp > 300 °C. IR (KBr, cm⁻¹): 3447 (NH), 3084 (CH_{arom.}), 2970, 2940 (CH_{aliph.}), 1672 (C=O_{triazine}), 1648 (C=O_{γ-pyrone}), 1636 (C=O_{quinolone}), 1612 (C=N) and 1588 (C=C). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 1.06 (t, 3H, *J*=7.5 Hz, CH₂CH₃), 2.17 (s, 3H, CH₃ triazine), 4.35 (q, 2H, CH₂CH₃), 7.40-7.75 (m, 3H, Ar-H), 8.14 (d, 1H, H-10), 8.65 (s, 1H, CH=N), 8.73 (s, 1H, H-2) and 13.68 (bs, 1H, NH exchangeable with D₂O). ¹³C NMR (DMSO-*d*₆, δ, 75 MHz): 12.3, 16.9, 38.1, 105.3, 115.4, 117.6, 121.8, 124.0, 125.8, 128.2, 135.1, 153.2, 156.5, 163.4, 165.2, 167.2, 168.9, 177.1, 183.4. Mass spectrum, *m/z* (*I*_r %): 409 (M⁺, 17), 376 (16), 366 (20), 349 (18), 338 (16), 310 (19), 266 (23), 240 (13), 212 (24), 187 (5), 161 (24), 158 (100), 142 (25), 133 (9), 130 (23), 119 (16), 117 (6), 91 (16), 89 (14) and 77 (6). Anal. Calcd for C₁₉H₁₅N₅O₄S (409.42); C, 55.74; H, 3.69; N, 17.11; S, 7.83%. Found: C, 55.49; H, 3.41; N, 16.89; S, 7.67%.

6-Ethyl-3-[(2-phenyl-4-oxoquinazolin-3-yl)imino]methyl]-4*H*-pyrano[3,2-*c*]quinoline-4,5(6*H*)-dione (20). A mixture of aldehyde **1** (0.54 g, 2 mmol) and 3-amino-2-phenylquinazolin-4(3*H*)-one (**18**) (0.47 g, 2 mmol) in absolute EtOH (20 mL) was heated under reflux for 30 min. The solid obtained during heating was filtered and crystallized from DMF/EtOH to give compound **20** as orange crystals, yield (0.50 g, 51%), mp 219-220 °C. IR (KBr, cm⁻¹): 3061 (CH_{arom.}), 2970, 2929 (CH_{aliph.}), 1679 (C=O_{quinazoline}), 1665 (C=O_{γ-pyrone}), 1630 (C=O_{quinolone}), 1603 (C=N) and 1588 (C=C). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 1.22 (t, 3H, *J*=7.2 Hz, CH₂CH₃), 4.25 (q, 2H, *J*=7.2 Hz, CH₂CH₃), 7.36 (t, 1H, *J*=7.8 Hz, Ar-H), 7.49 (d, 1H, *J*=6.6 Hz, Ar-H), 7.50-7.91 (m, 9H, Ar-H), 8.03 (d, 1H, *J*=8.7 Hz, Ar-H), 8.22 (d, 1H, *J*=7.8 Hz, Ar-H), 8.60 (s, 1H, CH=N) and 9.13 (s, 1H, H-2). Mass spectrum, *m/z* (*I*_r %): 487 (M⁺-1, 1), 266 (14), 240 (3), 238 (23), 222 (54), 194 (4), 187 (2), 172 (1), 145 (2), 132 (4), 119 (100), 91 (12), 77 (29) and 64 (16). Anal. Calcd for C₂₉H₂₀N₄O₄ (488.5); C, 71.20; H, 4.13; N, 11.47%. Found: C, 71.13; H, 4.08; N, 11.25%.

2-[(6-Ethyl-4,5-dioxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinolin-3-yl)methylidene]hydrazinecarbothioamide (21). A mixture of aldehyde **1** (0.54 g, 2 mmol) and thiosemicarbazide (0.18 g, 2 mmol) in EtOH (15 mL) was stirred at room temperature for 2 h. The solid so formed was filtered and crystallized from EtOH to give compound **21** as pale yellow crystals, mp 241-242 °C, yield (0.42 g, 61%). IR (KBr, cm⁻¹): 3416, 3273, 3158 (NH₂, NH), 2970, 2931 (CH_{aliph.}), 1677 (C=O_{γ-pyrone}), 1642 (C=O_{quinolone}), 1614 (C=N), 1589 (C=C) and 1287 (C=S). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 1.21 (t, 3H, *J*=6.9 Hz, CH₂CH₃), 4.33 (q, 2H, *J*=6.9 Hz, CH₂CH₃), 7.29 (t, 1H, *J*=7.5 Hz, H-9), 7.59 (d, 1H, *J*=7.8 Hz, H-7), 7.66 (t, 1H, *J*=8.1 Hz, H-8), 7.97 (s, 1H, CH=N), 8.09 (d, 1H, *J*=7.8 Hz, H-10), 8.82 (s, 1H, H-2), 9.82 (bs, 1H, NH exchangeable with D₂O), 13.40 (bs, 1H, NH exchangeable with D₂O) and 13.85 (bs, 1H, NH

exchangeable with D₂O). Anal. Calcd for C₁₆H₁₄N₄O₃S (342.37); C, 56.13; H, 4.12; N, 16.36; S, 9.37%. Found: C, 55.86; H, 4.03; N, 16.15; S, 9.28%.

2-Cyano-*N*'-[(6-ethyl-4,5-dioxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinolin-3-yl)-methylidene]aceto-hydrazide (22). A mixture of aldehyde **1** (0.54 g, 2 mmol) and cyanoacetohydrazide (0.20 g, 2 mmol) in absolute EtOH (15 mL) was stirred at room temperature for 1 h. The white precipitated so formed was filtered and crystallized from EtOH to give compound **22** as white crystals, yield (0.44 g, 63%), mp 222-223 °C. IR (KBr, cm⁻¹): 3447 (NH), 3097 (CH_{arom.}), 2980, 2923 (CH_{aliph.}), 2230 (C≡N), 1695 (C=O_{amide}), 1675 (C=O_{γ-pyrone}), 1651 (C=O_{quinolone}), 1598 (C=N) and 1566 (C=C). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 1.22 (t, 3H, *J*=7.2 Hz, CH₂CH₃), 4.00 (s, 2H, CH₂), 4.25 (q, 2H, *J*=7.2 Hz, CH₂CH₃), 7.31 (t, 1H, *J*=7.2 Hz, H-9), 7.59 (d, 1H, *J*=8.4 Hz, H-7), 7.73 (t, 1H, *J*=7.2 Hz, H-8), 8.12 (d, 1H, H-10), 8.26 (s, 1H, CH=N), 8.84 (s, 1H, H-2) and 11.55 (bs, 1H, NH exchangeable with D₂O). ¹³C NMR (DMSO-*d*₆, δ, 75 MHz): 12.6, 27.8, 38.5, 106.3, 115.4, 116.1, 117.2, 122.2, 124.3, 126.5, 128.6, 134.9, 154.3, 159.7, 162.1, 164.2, 170.8, 177.8. Mass spectrum, *m/z* (*I*_r %): 350 (M⁺, 8), 311 (3), 283 (71), 255 (15), 239 (6), 227 (4), 216 (5), 210 (3), 200 (5), 189 (5), 188 (13), 172 (26), 160 (18), 145 (12), 132 (45), 119 (33), 117 (10), 95 (100), 91 (15), 77 (65), 67 (74) and 65 (22). Anal. Calcd for C₁₈H₁₄N₄O₄ (350.33); C, 61.71; H, 4.03; N, 15.99%. Found: C, 61.54; H, 4.06; N, 15.75%.

Benzyl 2-[(6-ethyl-4,5-dioxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinolin-3-yl)methylidene]hydrazine-carbodithioate (23). A mixture of aldehyde **1** (0.54 g, 2 mmol) and *S*-benzyl dithiocarbamate (0.40 g, 2 mmol) in absolute EtOH (15 mL) was heated under reflux for 15 min. The solid so formed during heating was filtered and crystallized from AcOH to give compound **23** as yellow crystals, mp 199-200 °C, yield (0.49 g, 50%). IR (KBr, cm⁻¹): 3182 (NH), 2982, 2965 (CH_{aliph.}), 1655 (C=O_{γ-pyrone} and C=O_{quinolone}), 1616 (C=N), 1591 (C=C) and 1286 (C=S). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 1.22 (t, 3H, *J*=6.6 Hz, CH₂CH₃), 4.26 (q, 2H, *J*=7.2 Hz, CH₂CH₃), 4.62 (s, 2H, CH₂), 7.29-7.40 (m, 5H, Ar-H), 7.47 (d, 1H, *J*=7.8 Hz, Ar-H), 7.61 (d, 1H, *J*=8.7 Hz, H-7), 7.79 (t, 1H, *J*=7.5 Hz, H-8), 8.14 (d, 1H, *J*=7.8 Hz, H-10), 8.40 (s, 1H, CH=N), 9.23 (s, 1H, H-2) and 14.19 (bs, 1H, NH exchangeable with D₂O). Mass spectrum, *m/z* (*I*_r %): 449 (M⁺, 16), 372 (2), 283 (14), 254 (7), 238 (1), 216 (10), 187 (8), 172 (4), 160 (2), 145 (2), 132 (7), 119 (4), 117 (2), 104 (5), 95 (9), 91 (100), 77 (17) and 65 (22). Anal. Calcd for C₂₃H₁₉N₃O₃S₂ (449.55); C, 61.45; H, 4.26; N, 9.35; S, 14.27%. Found: C, 61.36; H, 4.21; N, 9.18; S, 14.17%.

***N,N*'-Bis[(6-ethyl-4,5-dioxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinolin-3-yl)methylidene]thiocarbo-hydrazide (24).** A mixture of aldehyde **1** (0.54 g, 2 mmol) and thiocarbohydrazide (0.11 g, 1 mmol) in EtOH was heated under reflux for 30 min. The solid obtained during heating was filtered and crystallized from AcOH to give compound **24** as pale yellow crystals, yield (0.41 g, 67%), mp 160-161 °C. IR (KBr, cm⁻¹): 3178 (NH), 2973, 2950 (CH_{aliph.}), 1653 (C=O_{γ-pyrone}), 1633 (C=O_{quinolone}), 1617 (C=N) and 1591 (C=C). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 1.21 (t, 6H, *J*=6.9 Hz, 2CH₂CH₃), 4.26 (q, 4H, *J*= 6.9 Hz, 2

CH₂CH₃), 7.29-7.43 (m, 2H, Ar-H), 7.59-7.67 (m, 2H, Ar-H), 7.30-7.81 (m, 2H, Ar-H), 8.08-8.17 (m, 2H, Ar-H), 8.35 (s, 2H, 2CH=N), 9.11 (s, 2H, 2H-2) and 14.09 (bs, 2H, 2NH exchangeable with D₂O). Mass spectrum, *m/z* (*I_r* %): 608 (M⁺, 35), 579 (24), 523 (24), 496 (38), 468 (38), 283 (27), 255 (22), 239 (28), 226 (32), 216 (15), 210 (6), 188 (23), 172 (28), 160 (16), 132 (68), 119 (22), 117 (31), 95 (100), 91 (35), 77 (99) and 64 (39). Anal. Calcd for C₃₁H₂₄N₆O₆S (608.62); C, 61.18; H, 3.97; N, 13.80; S, 5.27%. Found: C, 60.95; H, 3.68; N, 13.65; S, 5.23%.

1-Ethyl-4-hydroxy-3-(1*H*-pyrazol-4-ylcarbonyl)quinolin-2(1*H*)-one (25).

Method A. Compounds **21-24** (2 mmol) in aqueous pyridine (20 mmol) was heated under reflux for 30 min. After cooling at room temperature; the reaction mixture was poured onto ice-HCl. The solid obtained was filtered and crystallized from EtOH to give compound **25** as pale yellow crystals, mp > 300 °C.

Method B. A mixture of aldehyde **1** (0.54 g, 2 mmol) and hydrazine hydrate (0.1 mL, 2 mmol) in absolute EtOH was heated under reflux for 15 min. The solid obtained during heating was filtered and crystallized from EtOH to give compound **25** as pale yellow crystals, yield (0.32 g, 56%), mp > 300 °C. IR (KBr, cm⁻¹): 3420 (OH), 3143 (NH), 3008 (CH_{arom.}), 2961, 2931 (CH_{aliph.}), 1646 (C=O_{quinolone}), 1624 (C=O_{hydrogen bonded}), 1609 (C=N) and 1587 (C=C). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 1.21 (t, 3H, *J*=6.9 Hz, CH₂CH₃), 4.26 (q, 2H, *J*=6.9 Hz, CH₂CH₃), 7.33 (t, 1H, *J*=7.8 Hz, H-6), 7.59 (d, 1H, *J*=8.4 Hz, H-8), 7.73 (t, 1H, *J*=8.1 Hz, H-7), 8.09 (d, 1H, *J*=8.7 Hz, H-5), 8.14 (s, 1H, H-5_{pyrazole}), 8.38 (s, 1H, H-3_{pyrazole}), 13.39 (bs, 1H, NH exchangeable with D₂O) and 14.01 (bs, 1H, OH exchangeable with D₂O). ¹³C NMR (DMSO-*d*₆, δ, 75 MHz): 12.4, 38.1, 105.8, 110.7, 115.4, 121.5, 124.7, 126.1, 128.7, 134.3, 144.7, 144.8, 162.1, 168.7, 188.9. Mass spectrum, *m/z* (*I_r* %): 283 (M⁺, 21), 254 (13), 238 (22), 215 (8), 210 (9), 188 (16), 178 (100), 160 (2), 145 (11), 132 (27), 119 (26), 116 (14), 95 (31), 91 (16), 77 (50) and 64 (31). Anal. Calcd for C₁₅H₁₃N₃O₃ (283.28); C, 63.60; H, 4.63; N, 14.83%. Found: C, 63.43; H, 4.51; N, 14.72%.

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