Heteroannulated pyranoquinolinediones: Part 1. An efficient and convenient synthesis of the novel heteroannulated pyrano[3,2-*c*] quinoline-2,5(6*H*)-diones

Magdy A. Ibrahim* and Hany M. Hassanin

Department of Chemistry, Faculty of Education, Ain Shams University, Roxy, 11711, Cairo-Egypt
E-mail: magdy_ahmed1977@yahoo.com

DOI: http://dx.doi.org/10.3998/ark.5550190.p008.156

Abstract

The novel 3,4-dichloro-6-ethyl-2*H*-pyrano[3,2-*c*]quinoline-2,5(6*H*)-dione (**2**) was easily synthesized from chlorination of 6-ethyl-4-hydroxy-3-nitro-2*H*-pyrano[3,2-*c*]quinoline-2,5(6*H*)-dione (**1**). A variety of heteoannulated pyrano[3,2-*c*]quinoline derivatives were efficiently synthesized from the condensation reactions of compound **2** with some binucleophiles. The structures of the novel compounds were established by elemental analyses and spectral data.

Keywords: Chlorination, 3,4-dichloropyrano[3,2-*c*]quinoline-2,5(6*H*)-dione, heteroannulation, nucleophilic substitution.

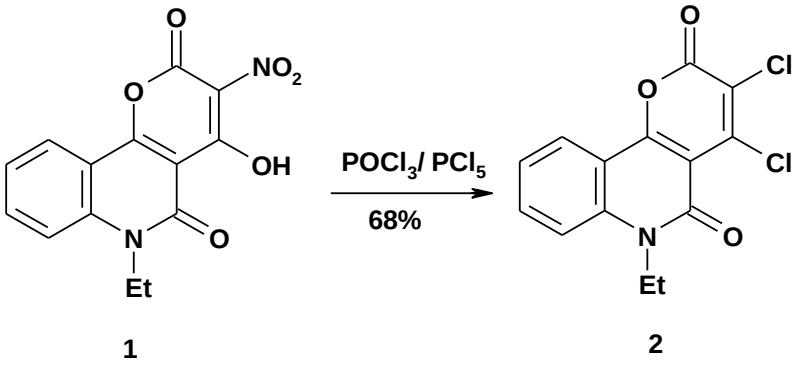
Introduction

Pyranoquinolinones constitute the parent ring structure of pyranoquinoline alkaloids which occur in the plant family *Rutaceae*. These pyranoquinoline alkaloids have gained considerable importance due to their pharmaceutical activities like anti-coagulant,[1] coronary constricting,[2] antifungal,[3] anti-histaminic, anti-allergic and anti-inflammatory.[4] Further, these pyranoquinolinones are also used as synthetic precursors for the synthesis of 4-hydroxyquinolin-2(1*H*)-ones and 3-acetyl-4-hydroxyquinolin-2(1*H*)-one derivatves.[5,6] A good deal of work has been done on the synthesis of these types of compounds with various substitutions in the aromatic ring.[7-9] On the other hand, *ortho*-dichloro heterocycles are good building blocks for the synthesis of fused heterocyclic compounds.[10-13] On the basis of the above observation and in continuation to our research work directed on the chemistry of pyrano[3,2-*c*]quinolinedione derivatives,[14-17] the present work aimed to synthesize the novel 3,4-dichloro-6-ethyl-2*H*-pyrano[3,2-*c*]quinoline-2,5(6*H*)-dione (**2**) as a starting material and study its chemical reactivity towards some 1,4-bifunctional nucleophiles, hoping to get a novel heteroannulated pyrano[3,2-*c*]

quinolinediones in which the bioactive pyrano[3,2-*c*]quinoline-2,5(6*H*)-dione ring system fused with a variety of heterocyclic compounds.

Results and Discussion

In the previous work,[18] chlorination of 6-ethyl-4-hydroxy-3-nitro-2*H*-pyrano[3,2-*c*]quinoline-2,5(6*H*)-dione (**1**)[14] using $POCl_3$ under mild conditions produced the corresponding chloro derivative, 4-chloro-3-nitro-6-ethyl-2*H*-pyrano[3,2-*c*]quinoline-2,5(6*H*)-dione. Herein, we found that chlorination of compound **1** using more strength conditions using a mixture of $POCl_3$ and PCl_5 produced the novel 3,4-dichloro-6-ethyl-2*H*-pyrano[3,2-*c*]quinoline-2,5(6*H*)-dione (**2**) in 68% yield (Scheme 1). Structure of dichloro derivative **2** was established from its correct elemental analysis and spectral data. The mass spectrum of compound **2** revealed the molecular ion peak at *m/z* 309, as the base peak, which agrees well with the molecular formula $C_{14}H_9Cl_2NO_3$. The spectrum also revealed M+2 and M+4 at *m/z* 311 and 313, respectively, as expected for compounds containing two chlorine atoms.

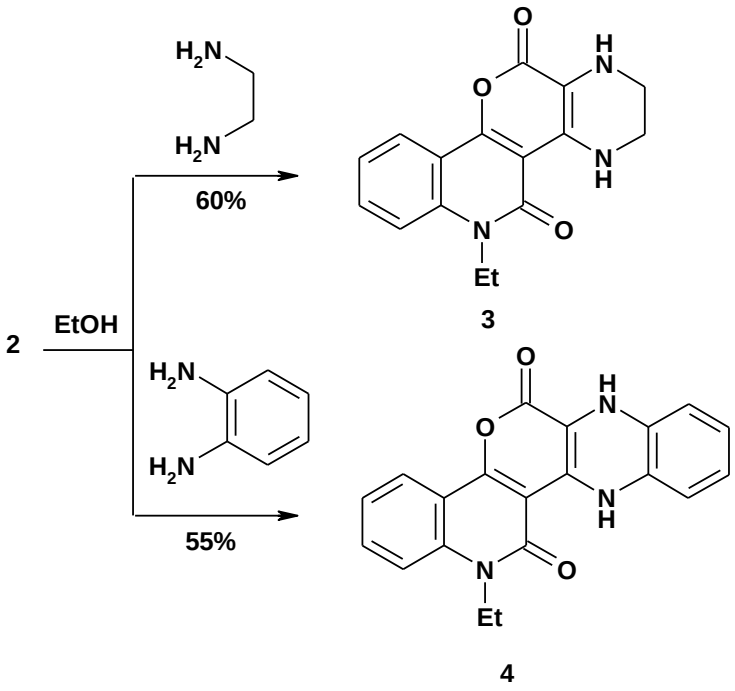


1 **2**

Scheme 1. Formation of the novel 3,4-dichloropyrano[3,2-*c*]quinolinedione **2**.

The dichloro derivative **2**, as 1,2-bifunctional electrophiles, represents a good building block for the synthesis of a series of heteroannulated pyrano[3,2-c]quinolinediones, *via* its condensation reactions with a variety of 1,4-bifiunctional nucleophiles. Thus, condensation of compound **2** with ethylenediamine and *o*-phenylenediamine in absolute ethanol produced the heteroannulated pyrano[3,2-*c*]quinolinediones **3** and **4**, respectively (Scheme 2). The elemental analyses agree well with the molecular formula for compounds **3** and **4** which prove the elimination of the two chlorine atoms during the reaction. These reactions may proceed initially *via* nucleophilic attack at C-4 position with elimination of a molecule of HCl (C-4 is more electron deficient, β position of α,β-unsaturated ketone) followed by nucleophilic attack by the other amino group at C-3 with elimination of another molecule of HCl. The ^{1}H NMR spectrum of compound **3** showed characteristic singlet signals at δ 3.72 and 3.75 ppm attributed to the

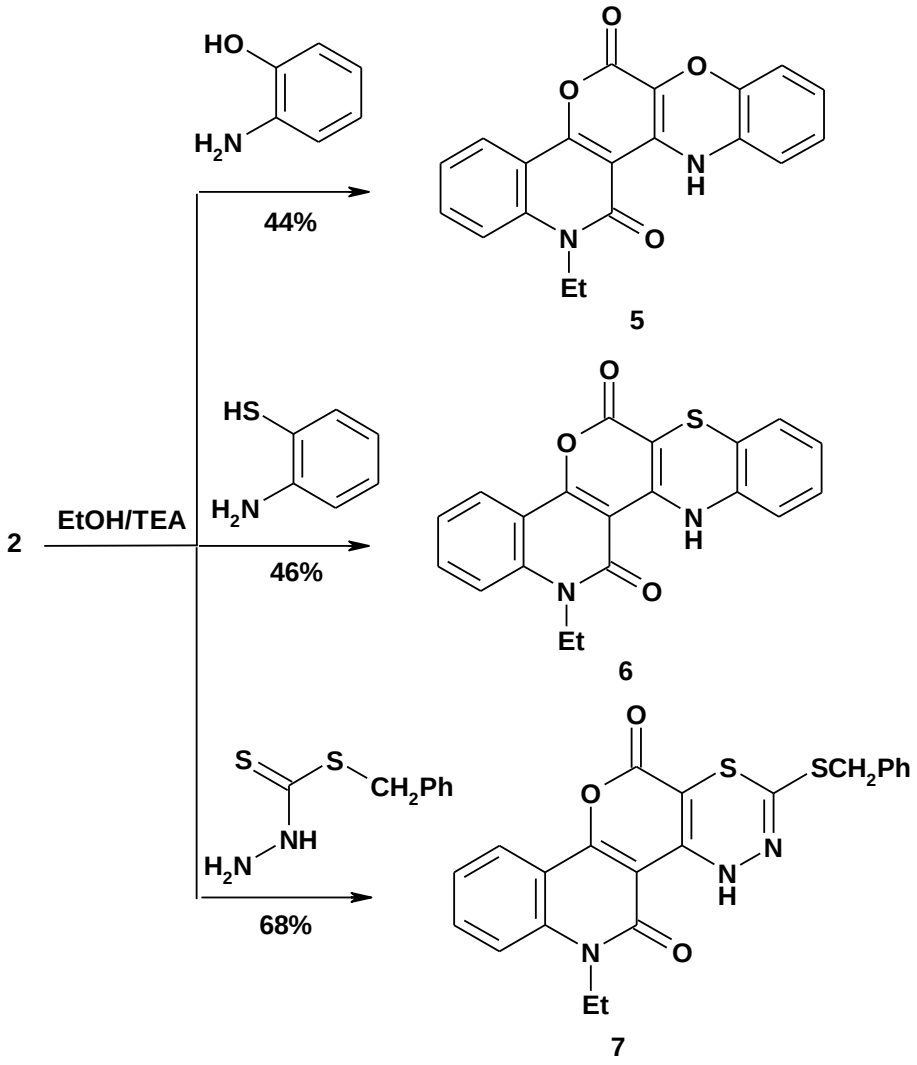
2CH_2 protons. Also, the mass spectrum of compound **4** showed the molecular ion peak at *m/z* 345 which agrees well with the molecular formula $C_{20}H_{15}N_3O_3$ and supports the identity of structure.



Scheme 2. Condensation of **2** with ethylenediamine and *o*-phenylenediamine.

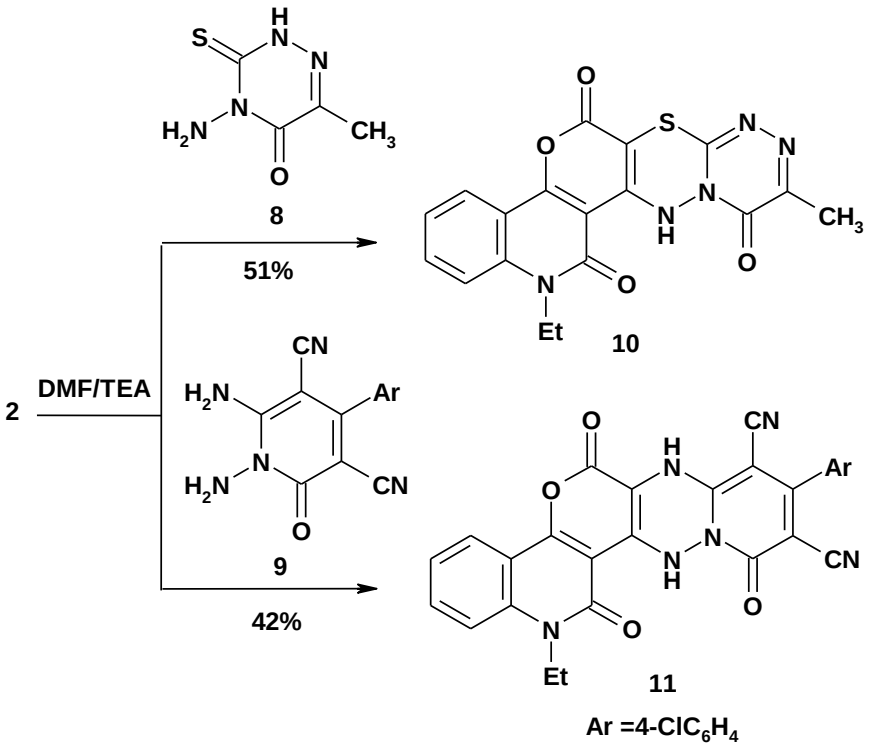
The reaction of dichloro derivative **2** was studied towards a variety of unsymmetrical bifunctional nucleophiles. Thus, condensation of compound **2** with 2-aminophenol and 2-aminothiophenol in absolute ethanol containing few drops of triethylamine (TEA) gave the heteroannulated pyrano[3,2-*c*]quinolinedione derivatives **5** and **6**, respectively (Scheme 3). These reactions may proceed *via* nucleophilic attack of NH_2 group at C-4 position with elimination of HCl followed by heterocyclization with loss of another molecule of HCl. The ^{1}H NMR spectra of compounds **5** and **6** showed an exchangeable signals attributed to the NH protons at δ 9.86 and 10.84 ppm, respectively. Structure of compound **5** was further deduced from its mass spectrum which revealed the molecular ion peak at *m/z* 346 which agrees well with the formula weight (346.35) and supports the structure.

Condensation of compound **2** with *S*-benzyl dithiocarbazate, under the same reaction conditions, produced quinolino[3',4':5,6]pyrano[3,4-*e*][1,3,4]thiadiazine derivative **7** (Scheme 3). Its ^{1}H NMR spectrum showed characteristic singlet at δ 4.46 ppm attributed to the SCH_2 protons.



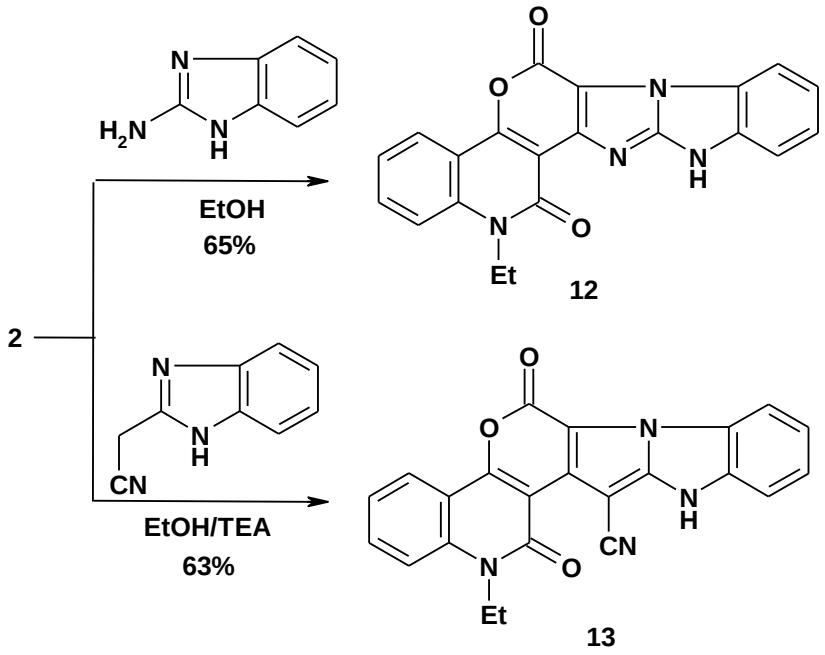
Scheme 3. Formation of the heteroannulated pyranoquinolinediones **5**-**7**.

The present study was extended to obtain some new heterocyclic systems fused with the pyrano[3,2-*c*]quinolinedione ring system. Thus, condensation of compound **2** with 4-amino-6-methyl-3-thioxo-3,4-dihydro-1,2,4-triazin-5(2*H*)-one (**8**)[19] and 1,6-diamino-4-(4-chlorophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile (**9**)[20] in boiling DMF containing few drops of TEA afforded the novel quinolino[3",4":5',6']pyrano[3',4'-*e*][1,2,4]triazino[1,2-*b*] [1,3,4]thiadiazine **10** and quinolino[3",4":5',6']pyrano[3',4'-*e*]pyrido[1,2-*b*][1,2,4]triazine **11**, respectively (Scheme 4). The ^{1}H NMR spectrum of compound **10** showed characteristic singlet signal attributed to the $CH_{3\ triazine}$ protons at δ 3.52 ppm, while the IR spectrum of compound **11** showed characteristic absorption bands at 2211 (C≡N), 1737 (OC=O) and 1641 ($C{=}O_{pyridine\ and\ quinoline}$) cm^{-1}.



Scheme 4. Formation of the heteroannulated pyranoquinolinediones **10** and **11**.

Compound **2** reacts with 2-aminobenzimidazole and benzimidazol-2-ylacetonitrile to produce the novel heteroannulated quinolino[3",4":5',6']pyrano[3',4':5,4]imidazo[1,2-*a*] benzimidazole **12** and quinolino[3",4":5',6']pyrano[3',4':5,4]pyrrolo[1,2-*a*]benzimidazole **13**, respectively (Scheme 5). IR spectrum of compound **12** showed characteristic absorption bands at 3362 (NH), 1690 (OC=O and $C=O_{quinolinone}$) cm^{-1}, while the IR spectrum of compound **13** showed characteristic absorption bands at 3441 (NH), 2213 (C≡N), 1733 (OC=O), 1685 ($C=O_{quinolinone}$) cm^{-1}. The ^1H NMR spectra of compounds **12** and **13** showed signals attributed to the ethyl and eight aromatic protons, in addition to an exchangeable signals attributed to the NH protons at δ 11.33 and 11.65 ppm, respectively. Also, the mass spectrum of compound **12** showed the molecular ion peak at *m/z* 370 which agrees well with the formula weight (370.36) and supports the identity of structure.



Scheme 5. Formation of the heteroannulated pyranoquinolinediones **12** and **13**.

Conclusions

In the present work, the novel 3,4-dichloro-6-ethyl-2*H*-pyrano[3,2-*c*]quinoline-2,5(6*H*)-dione (**2**) was efficiently synthesized and utilized as a good precursor to obtain a variety of novel annulated heterocyclic systems containing pyrano[3,2-*c*]quinolinedione moiety.

Experimental Section

General. Melting points were determined on a digital Stuart SMP3 apparatus. Infrared spectra were measured on Perkin-Elmer 293 spectrophotometer (cm^{-1}), using KBr disks. ^{1}H NMR spectra were measured on Jeol Eca-(500MHz), and/or Mercury-300BB (300MHz), using DMSO-d_6 as a solvent and TMS (δ) as the internal standard. ^{13}C NMR spectra were measured on Mercury-300BB (75 MHz), using DMSO-d_6 as a solvent and TMS (δ) as the internal standard. Mass spectra were obtained using GC-2010 Shimadzu Gas chromatography mass spectrometry instrument (70 eV). Elemental microanalyses were performed on a Perkin–Elmer CHN-2400 analyzer.

3,4-Dichloro-6-ethyl-2*H*-pyrano[3,2-*c*]quinoline-2,5(6*H*)-dione (2). A mixture of compound **1** (3.02 g, 10 mmol) in phosphorus oxychloride (10 mL) and phosphorus pentachloride (3 g, 15 mmol) was heated under reflux for 4h, or till the evaporation of the brown vapors ceased. After cooling, the reaction mixture was poured onto crushed ice. The precipitate so formed was filtered

off, washed with water and crystallized from ethanol to afford compound **2** as yellow crystals mp 208-209 ºC, yield 2.1 g (68%). IR (KBr, cm^{-1}): 3060 ($CH_{arom.}$), 2976, 2930 ($CH_{aliph.}$), 1739 (OC=O), 1635 ($C=O_{quinolinone}$), 1570 (C=C), 759 (C-Cl). ^{1}H NMR (DMSO-d_6, δ): 1.17 (t, 3H, *J* 6.9 Hz, CH_2CH_3), 4.27 (q, 2H, *J* 6.9 Hz, CH_2CH_3), 7.21 (t, 1H, *J* 7.6 Hz, H-9), 7.49 (d, 1H, *J* 8.4 Hz, H-7), 7.58 (t, 1H, *J* 6.8 Hz, H-8), 8.04 (d, 1H, *J* 7.6 Hz, H-10). ^{13}C NMR (DMSO-d_6, δ): 13.3 (CH_3), 38.0 (CH_2), 113.3, 117.0, 118.9, 124.4, 124.7, 125.5, 136.4, 138.9, 154.2, 159.4, 164.0, 166.4. *m/z* (*I*%): 313 (M+4; 10), 311 (M+2; 63), 309 (M^+; 100), 281 (62), 266 (9), 253 (57), 218 (3), 197 (15), 161 (3), 146 (8), 132 (7), 77 (2). Anal. Calcd for $C_{14}H_9Cl_2NO_3$ (310.13): C, 54.22; H, 2.93; N, 4.52%. Found C, 54.40; H, 2.40; N, 4.70%.

11-Ethyl-1,2,3,4-tetrahydroquinolino[3',4':5,6]pyrano[3,4-*b*]pyrazine-5,12(6*H*,11*H*)-dione (3). A mixture of compound **2** (0.62 g, 2 mmol) and ethylenediamine (0.12 g, 2 mmol) in absolute ethanol was heated under reflux for 15 min. The yellow crystals obtained after cooling were filtered off and recrystallized from ethanol to give compound **3** as yellow crystals, mp 272-273 ºC, yield 0.36 g (60%). IR (KBr, cm^{-1}): 3437 (2NH), 3070 ($CH_{arom.}$), 2935, 2865 ($CH_{aliph.}$), 1730 (OC=O), 1660 ($C=O_{quinolinone}$), 1604 (C=C). ^{1}H NMR (DMSO-d_6, δ): 1.15 (t, 3H, CH_2CH_3), 3.72 (s, 2H, CH_2), 3.75 (s, 2H, CH_2), 4.22 (q, 2H, CH_2CH_3), 6.25 (bs, 2H, 2NH exchangeable with D_2O), 7.30 (t, 1H, *J* 8.4 Hz, H-8), 7.51 (d, 1H, *J* 8.8 Hz, H-10), 7.71 (t, 1H, *J* 7.2 Hz, H-9), 8.07 (d, 1H, *J* 7.8 Hz, H-7). Anal. Calcd for $C_{16}H_{15}N_3O_3$ (297.31): C, 64.64; H, 5.09; N, 14.13%. Found C, 64.33; H, 4.75; N, 13.86 %.

14-Ethyl-7,12-dihydroquinolino[3',4':5,6]pyrano[3,4-*b*]quinoxaline-6,13(5*H*,14*H*)-dione (4). A mixture of compound **2** (0.62 g, 2 mmol) and *o*-phenylenediamine (0.22 g, 2 mmol) in absolute ethanol was heated under reflux for 15 min. The yellow crystals obtained during heating were filtered off and recrystallized from DMF/EtOH to give compound **4** as yellow crystals, mp 292-293 ºC, yield 0.38 g (55%). IR (KBr, cm^{-1}): 3442 (2NH), 3082 ($CH_{arom.}$), 2977, 2930 ($CH_{aliph.}$), 1736 (OC=O), 1670 ($C=O_{quinoline}$), 1567 (C=C). ^{1}H NMR (DMSO-d_6, δ): 1.23 (t, 3H, *J* 6.0 Hz, CH_3), 4.35 (q, 2H, *J* 6.0 Hz, CH_2), 6.69 (t, 1H, Ar-H), 6.84 (d, 1H, Ar-H), 6.95-7.03 (m, 2H, Ar-H), 7.47 (t, 1H, Ar-H), 7.79 (d, 1H, Ar-H), 7.88 (t, 1H, Ar-H), 8.13 (d, 1H, Ar-H), 11.55 (s, 1H, NH exchangeable with D_2O), 12.40 (s, 1H, NH exchangeable with D_2O). *m/z* (*I*%): 345 (72), 317 (17), 302 (44), 291 (100), 214 (26), 188 (20), 172 (45), 146 (46), 132 (52), 116 (44), 105 (22), 91 (25), 77 (89), 65 (27). Anal. Calcd for $C_{20}H_{15}N_3O_3$ (345.35): C, 69.56; H, 4.38; N, 12.17%. Found C, 69.84; H, 4.26; N, 12.11%.

14-Ethyl-12-hydroquinolino[3',4':5,6]pyrano[3,4-*b*]benzoxazine-6,13(5*H*,14*H*)-dione (5). A mixture of compound **2** (0.62 g, 2 mmol) and 2-aminophenol (0.22 g, 2 mmol), in absolute ethanol containing few drops of triethyl amine, was heated under reflux for 2h. The solid so formed after cooling was filtered off and crystallized from methanol to give compound **5** as pale brown crystals, mp 245-246 ºC, yield 0.31 g (44%). IR (KBr, cm^{-1}): 3433 (NH), 3085 ($CH_{arom.}$), 2980, 2923 ($CH_{aliph.}$), 1746 (OC=O), 1630 ($C=O_{quinoline}$), 1581 (C=C). ^{1}H NMR (DMSO-d_6, δ): 1.25 (t, 3H, *J* 7.2 Hz, CH_3), 4.27 (q, 2H, *J* 7.8 Hz, CH_2), 6.81 (t, 1H, *J* 7.8 Hz, Ar-H), 7.04 (d, 1H, *J* 6.6 Hz, Ar-H), 7.12-7.37 (m, 1H, Ar-H), 7.53 (t, 1H, *J* 6.6 Hz, Ar-H), 7.60 (d, 1H, *J* 8.4 Hz, Ar-H), 7.69-7.99 (m, 2H, Ar-H), 8.19 (d, 1H, *J* 8.4 Hz, Ar-H), 9.86 (s, 1H, NH exchangeable

with D_2O). *m/z* (*I*%): 346 (67), 255 (71), 207 (67), 161 (24), 149 (83), 134 (62), 121 (17), 91 (100), 77 (74). Anal. Calcd for $C_{20}H_{14}N_2O_4$ (346.35): C, 69.36; H, 4.07; N, 8.09%. Found: C, 68.89; H, 4.18; N, 7.84%.

14-Ethyl-12-hydroquinolino[3',4':5,6]pyrano[3,4-*b*]benzothiazine-6,13(5*H*,14*H*)-dione (6). A mixture of compound **2** (0.62 g, 2 mmol) and 2-aminothiophenol (0.24 mL, 2 mmol), in absolute ethanol containing few drops of triethyl amine, was heated under reflux for 2h. The precipitate so formed after cooling was filtered off and crystallized from ethanol to give compound **6** as yellow crystals, mp 226-227 ºC, yield 0.33 g (46 %). IR (KBr, cm^{-1}): 3437 (NH), 3064 ($CH_{arom.}$), 2974, 2925 ($CH_{aliph.}$), 1702 (OC=O), 1621 ($C=O_{quinoline}$), 1558 (C=C). ^1H NMR (DMSO-d_6, δ): 1.26 (t, 3H, *J* 6.6 Hz, CH_3), 4.28 (q, 2H, *J* 6.6 Hz, CH_2), 6.76-7.94 (m, 7H, Ar-H), 8.08 (d, 1H, *J* 7.5 Hz, Ar-H), 10.84 (s, 1H, NH exchangeable with D_2O). ^{13}C NMR (DMSO-d_6, δ): 12.7 (CH_3), 37.2 (CH_2), 110.8, 113.5, 115.2, 116.9, 120.5, 120.6, 123.3, 125.6, 126.5, 127.8, 132.5, 133.7, 135.1, 135.3, 149.2, 156.2, 157.8, 174.5. Anal. Calcd for $C_{20}H_{14}N_2O_3S$ (362.41): C, 66.28; H, 3.89; N, 7.73; S, 8.85%. Found C, 66.67; H, 4.30; N, 7.29; S, 8.59%.

6-Ethyl-2-benzylthio-4*H*-quinolino[3',4':5,6]pyrano[3,4-*e*][1,3,4]thiadiazine-5,12(6*H*,11*H*)-dione (7). A mixture of compound **2** (0.62 g, 2 mmol) and *S*-benzyl dithiocarbazate (0.40 g, 2 mmol), in absolute ethanol (30 mL) containing few drops of triethyl amine, was heated under reflux for 3h. The precipitate so formed during heating was filtered off and crystallized from DMF to give compound **7** as yellow crystals, mp > 300 ºC, yield 0.59 g (68%). IR (KBr, cm^{-1}): 3447 (NH), 2931, 2840 ($CH_{aliph.}$), 1716 (OC=O), 1647 ($C=O_{quinoline}$), 1615 (C=N), 1596 (C=C). ^1H NMR (DMSO-d_6, δ): 1.15 (t, 3H, *J* 7.6 Hz, CH_3), 4.21 (q, 2H, *J* 7.6 Hz, CH_2), 4.46 (s, 2H, CH_2Ph), 7.32-7.45 (m, 4H, Ar-H), 7.55 (d, 1H, *J* 7.6 Hz, Ar-H), 7.71-7.83 (m, 3H, Ar-H), 8.02 (d, 1H, Ar-H), 8.25 (bs, 1H, NH exchangeable with D_2O). Anal. Calcd for $C_{22}H_{17}N_3O_3S_2$ (435.52): C, 60.67; H, 3.93; N, 9.65; S, 14.72%. Found C, 60.45; H, 3.68; N, 9.58; S, 14.45%.

8-Ethyl-3-methyl-6*H*-quinolino[3'',4'':5',6']pyrano[3',4'-*e*][1,2,4]triazino[1,2-*b*][1,3,4] thiadiazine-4,7,14 (4*H*,8*H*,13*H*)-trione (10). A mixture of compound **2** (0.62 g, 2 mmol) and 4-amino-6-methyl-3-thioxo-3,4-dihydro-1,2,4-triazin-5(2*H*)-one (**8**) (0.32 g, 2 mmol), in DMF containing few drops of triethylamine, was heated under reflux for 3h. The precipitate so formed after cooling was filtered off and crystallized from DMF to give compound **10** as yellow crystals, mp > 300 ºC, yield 0.41 g (51%). IR (KBr, cm^{-1}): 3446 (NH), 3020 ($CH_{arom.}$), 2976, 2931 ($CH_{aliph.}$), 1733 (OC=O), 1716 ($C=O_{triazine}$), 1634 ($C=O_{quinoline}$), 1584 (C=N), 1558 (C=C). ^1H NMR (DMSO-d_6, δ): 1.17 (t, 3H, CH_3), 3.52 (s, 3H, $CH_{3\ triazine}$), 4.25 (q, 2H, CH_2), 7.38 (bs, 1H, Ar-H), 7.65-7.76 (m, 2H, Ar-H), 8.06 (bs, 1H, Ar-H), 11.34 (bs, 1H, NH exchangeable with D_2O). Anal. Calcd for $C_{18}H_{13}N_5O_4S$ (395.39): C, 54.68; H, 3.31; N, 17.71; S, 8.11%. Found: 54.74; H, 3.35; N, 17.49; S, 7.94%.

2-(4-Chlorophenyl)-8-ethyl-4,7,14-trioxo-4,6,8,13,15-pentahydroquinolino[3'',4'':5',6'] pyrano[3',4'-*e*]pyrido[1,2-*b*][1,2,4]triazine-1,3-dicarbonitrile (11). A mixture of compound **2** (0.62 g, 2 mmol) and 1,6-diamino-4-(4-chlorophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile (**9**) (0.56 g, 2 mmol), in DMF (10 mL) containing two drops of triethylamine, was heated under reflux for 3h. The precipitate so formed during heating was filtered off and

crystallized from DMF to give compound **11** as yellow crystals, mp > 300 °C, yield 0.44 g (42%). IR (KBr, cm^{-1}): 3393, 3263 (2NH), 2979, 2920, 2845 ($CH_{aliph.}$), 2211 (2C≡N), 1737 (OC=O), 1641 ($C=O_{pyridine}$ and $C=O_{quinoline}$), 1600 (C=C). ^{1}H NMR (DMSO-d_6, δ): 1.22 (t, 3H, *J* 6.9 Hz, CH_3), 4.33 (q, 2H, *J* 6.9 Hz, CH_2), 5.62 (bs, 1H, NH exchangeable with D_2O), 7.48 (t, 1H, Ar-H), 7.61 (d, 2H, Ar-H), 7.83-7.90 (m, 2H, Ar-H), 8.02 (d, 2H, Ar-H), 8.08 (d, 1H, Ar-H), 13.77 (bs, 1H, NH exchangeable with D_2O). Anal. Calcd for $C_{27}H_{15}ClN_6O_4$ (522.89): C, 62.02; H, 2.89; N, 16.07%. Found C, 62.27; H, 2.68; N, 16.02%.

15-Ethyl-12*H*-quinolino[3'',4'':5',6']pyrano[3',4':5,4]imidazo[1,2-*a*]benzimidazole-6,14(5*H*,15H)-dione (12). A mixture of compound **2** (0.62 g, 2 mmol) and 2-amino benzimidazole (0.26 g, 2 mmol) in absolute ethanol (20 mL) was heated under reflux for 30 min. The precipitate so formed during heating was filtered off and crystallized from DMF/H_2O to give compound **12** as yellow crystals, mp > 300 °C, yield 0.48 g (65%). IR (KBr, cm^{-1}): 3362 (NH), 3122 ($CH_{arom.}$), 2950, 2884 ($CH_{aliph.}$), 1690 (OC=O and $C=O_{quinoline}$), 1604 (C=N), 1522 (C=C). ^{1}H NMR (DMSO-d_6, δ): 1.16 (t, 3H, CH_3), 4.20 (q, 2H, CH_2), 7.20 (t, 1H, Ar-H), 7.35 (d, 1H, Ar-H), 7.37 (d, 1H, Ar-H), 7.62-7.63 (m, 2H, Ar-H), 7.82-7.85 (m, 2H, Ar-H), 8.12 (d, 1H, Ar-H), 11.33 (bs, 1H, NH exchangeable with D_2O). *m/z* (*I*%): 370 (14), 244 (10), 216 (14), 206 (10), 133 (100), 116 (14), 105 (30), 91 (27), 77 (8). Anal. Calcd for $C_{21}H_{14}N_4O_3$ (370.36): C, 68.10; H, 3.81; N, 15.13%. Found 68.46; H, 3.56; N, 15.02%.

15-Ethyl-6,14-dioxo-5,15-dihydro-12*H*-quinolino[3'',4'':5',6']pyrano[3',4':5,4]pyrrolo[1,2-*a*]benzimidazole-13-carbonitrile (13). A mixture of compound **2** (0.62 g, 2 mmol) and benzimidazol-2-ylacetonitrile (0.32 g, 2 mmol), in absolute ethanol (20 mL) containing two drops of triethylamine, was heated under reflux for 1h. The precipitate so formed after cooling was filtered off and crystallized from DMF to give compound **13** as yellow crystals, mp > 300 °C, yield 0.50 g (63%). IR (KBr, cm^{-1}): 3441 (NH), 3080 ($CH_{arom.}$), 2978, 2937 ($CH_{aliph.}$), 2213 (C≡N), 1733 (OC=O), 1685 ($C=O_{quinoline}$), 1636 (C=N), 1557 (C=C). ^{1}H NMR (DMSO-d_6, δ): 1.18 (t, 3H, CH_3), 4.27 (q, 2H, CH_2), 7.40 (t, 1H, Ar-H), 7.44 (d, 1H, Ar-H), 7.68 (d, 1H, Ar-H), 7.76 (t, 1H, Ar-H), 7.79-7.89 (m, 2H, Ar-H), 8.08-8.12 (m, 2H, Ar-H), 11.65 (bs, 1H, NH exchangeable with D_2O). Anal. Calcd for $C_{23}H_{14}N_4O_3$ (394.38): C, 70.05; H, 3.58, N, 14.21%. Found 69.60; H, 3.60, N, 14.04%.

References

1. Anniyappan, M.; Muralidhran, D.; Perumal, P. T. *Tetrahedron Lett.* **2003**, *44*, 3653. http://dx.doi.org/10.1016/S0040-4039(03)00707-X
2. Ravindranath, N.; Ramesh, C.; Reddy, M. R.; Das, B. *Chem. Lett.* **2003**, *3*, 222. http://dx.doi.org/10.1246/cl.2003.222
3. Badhwar, I. C.; Venkataraman, K. *J. Chem. Soc.* **1932**, 2420. http://dx.doi.org/10.1039/jr9320002420

4. Chen, I. S.; Wu, S. J.; Tsai, I. L.; Wu, T. S.; Pezzuto, J. M.; Lu, M. C.; Chai. H.; Suh, N.; Teng C. M. *J. Nat. Prod.* **1994**, *57*, 1206. http://dx.doi.org/10.1021/np50111a003
5. Kappe, T. *Farmaco* **1999**, *54*, 309. http://dx.doi.org/10.1016/S0014-827X(99)00030-0
6. Abass, M.; Othman, E. S. *Synth. Commun*. **2001**, *31*, 3361. http://dx.doi.org/10.1081/SCC-100106047
7. Huffman, J. W.; Hsu, T. M. *Tetrahedron Lett*. **1972**, *13*, 141. http://dx.doi.org/10.1016/S0040-4039(01)84261-1
8. Groot, A.; Jansen, B. J. M. *Tetrahedron Lett.* **1975**, *16*, 3407. http://dx.doi.org/10.1016/S0040-4039(00)91410-2
9. Bowman, R. M.; Grundon, M. F.; James K. J. *J. Chem. Soc. Perkin Trans. 1* **1973**, 1055.
10. Prasanna, B.; Srinivas, B.; Jagannadham, Y.; Rao, S. A. *E- J. Chem*. **2012**, *9*, 893.
11. Dabholkar, V. V.; Patil, S. R.; Pandey, R. V. *Heterocycl. Lett*. **2012**, *2*, 129.
12. Keivanloo, A.; Bakherad, M. *Synthesis* **2010**, *10*, 1599. http://dx.doi.org/10.1055/s-0029-1218715
13. Volovenko, Y. M.; Dubinina, G. G. *Chem. Heterocycl. Compds.* **2002**, *38*, 219. http://dx.doi.org/10.1023/A:1015399511473
14. Ibrahim, M. A.; Hassanin, H. M.; Gabr, Y. A.; Alnamer, Y. A. *J. Braz. Chem. Soc*. **2012**, *23*, 905. http://dx.doi.org/10.1590/S0103-50532012000500016
15. Hassanin, H. M.; Ibrahim, M. A.; Gabr, Y. A.; Alnamer, Y. A. *J. Heterocycl. Chem*. **2012**, *49*, 1269. http://dx.doi.org/10.1002/jhet.906
16. Hassanin, H. M.; Ibrahim, M. A.; Alnamer, Y. A. *Turkish J. Chem*. **2012**, *36*, 682.
17. Ibrahim, M. A.; Hassanin, H. M.; Gabr, Y. A.; Alnamer, Y. A. *Eur. J. Chem*. **2010**, *3*, 195. http://dx.doi.org/10.5155/eurjchem.1.3.195-199.91
18. Hassanin, H. M. *Arkivoc* **2012**, (vi), 384. http://dx.doi.org/10.3998/ark.5550190.0013.634
19. Dornow, A.; Menzel, M. P. *Chem. Ber*. **1964**, *97*, 2173. http://dx.doi.org/10.1002/cber.19640970811
20. Al-Najjar, A. A. A.; Amer, S. A. R.; Riad, M.; Elghamy, I.; Elnagdi, M. H. *J. Chem. Res.(S)* **1996**, 296.

