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ORIGINAL PAPER

Synthesis of spiro[indoline-3,4′-pyrano[3,2-*c*]quinolone]-3′-carbonitriles

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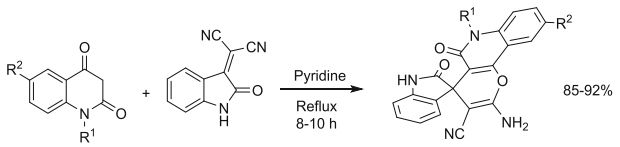
Abstract Quinoline-2,4-diones reacted with 2-(2-oxo-1,2-dihydroindol-3-ylidene)malononitrile in pyridine to give 2′-amino-2,5′-dioxo-5′,6′-dihydrospiro(indoline-3,4′-pyrano[3,2-*c*]quinoline)-3′-carbonitriles in good to excellent yields. The structures of all new products were proven using one- and two-dimensional NMR, IR, and mass spectral data, and in five cases X-ray structural analyses. The possible mechanism for the reaction is also discussed.

Graphical abstract



Keywords Quinolin-2,4-diones · Isatinemalononitrile · Spiro-compounds · X-ray analysis

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Introduction

Great efforts have been made to synthesis, characterize, and investigate the biological activities of spiro-compounds. They possess very promising biological activities as anticonvulsant [1–3], antibacterial [4], anti-Alzheimer [5, 6], antimicrobial [7], anti-dermatities [8], anticancer [9], and pain relief [10, 11], in addition to their medical, agricultural, and industrial uses [12–15]. Therefore, spiro-compounds have drawn tremendous interest of researchers in synthetic organic chemistry and medicinal chemistry. Indeed, quinolones represent a class of fused ring systems with interesting essential role in the construction of many bioactive compounds, that they can exhibit antibacterial [16], antifungal [16], antitumor [17], anticancer [18], anti-tuberculosis [18], antibiotic [19, 20], antimicrobial [21–23], anti-inflammatory activities [21–23]. However, they have herbicides [24], and insecticide agents [25]. On the other hand, isatinemalononitrile is a scaffold for the synthesis of fused spiro-compounds [26–32], many of its derivatives are potent inhibiting caspase [33]. The heterocyclic spiro-oxindole framework is an important structural motif in natural products which can act as potent non-peptide inhibitors [34, 35]. These compounds are very interesting: they can act as antibacterial and anti-HIV agents [36], and exhibit biological activities [37], such as antitumor and anticancer [38] and cellular evaluation [39]. To extend the knowledge around the new spiro-compounds, we focused our searches to synthesis a new class of them which we expect they will have important activities in medicinal and industrial area. Previously, Aly et al. synthesized fused spiro-pyranoindanoparacyclophanes [40], spiro-pyridazino-cyclohexadiene as well as spiro-thiadiazolo-pyrimidinocyclohexadiene derivatives [41],

and spiro(indole-3,3′-[1,2,4]-triazol)-2(1*H*)-ones [42]. We have also recently investigated the reaction of 2,4-quinolones with dialkyl acetylenedicarboxylates. The reaction gave ethyl 5,6-dihydro-2,5-dioxo-6,9-disubstituted-2*H*-pyrano[3,2-*c*]quinoline-4-carboxylates and dialkyl 2-(4-oxo-1,4-dihydro-quinolin-3-yl)fumarates in good yields [43]. So and herein, we describe the synthesis of a class of new spiro-compounds, via the reaction of quinoline-2,4-(1*H*,3*H*)-diones **1a**–**1f** with 2-(2-oxo-1,2-dihydroindol-3-ylidene)malononitrile (**2**).

Results and discussion

Refluxing equimolar amounts of 1,6-disubstituted quinoline-2,4-(1*H*,3*H*)-diones **1a**–**1f** with 2-(2-oxo-1,2-dihydroindol-3-ylidene)malononitrile (**2**) in dry pyridine solution led to the formation of spiro[indoline-3,4′-pyrano[3,2-*c*]quinolone]-3′-carbonitriles **3a**–**3f** in 85–92% yields (Scheme 1).

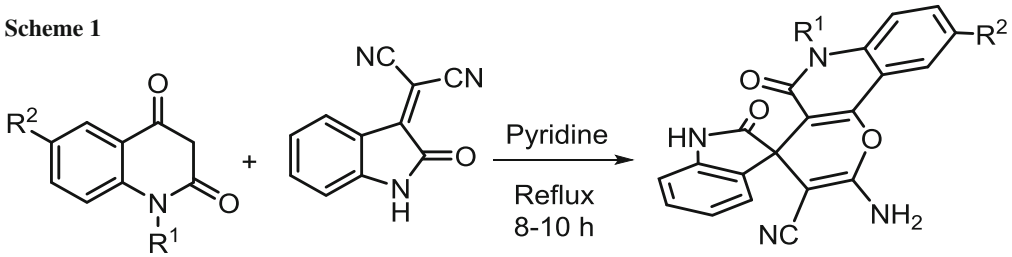
To confirm the structures of all the obtained products, elemental analyses, IR, NMR (^{1}H, ^{13}C, 2D NMR, ^{15}N) and mass spectra were performed; these and elemental analyses were in good agreement with the assigned structures. As an example, the structure of compound **3a** which was previously prepared [21f]. However, its detailed NMR data were not extensively reported. The NMR spectra of **3a** (Table 1) showed a broad 1H singlet at $\delta = 11.75$ ppm, assigned as NH-6′. This proton gives HSQC correlation with N-6, and gives HMBC correlation with C-2′, C-3′, C-3, 4′, C-5′, C-9′, C-10′, and C-10′b. The distinctive hydrogens and carbons of compound **3a** were shown in Fig. 1. Whilst, the structure assignment of **3a** is unambiguously confirmed by an X-ray crystal structure as shown in Fig. 2.

On the other side, the structure assignments of **3b**–**3d** followed from single-crystal X-ray analyses were found bonded to DMF as the solvent of recrystallization (Figs. 3, 4, 5).

Another representative example, named 2′-amino-6′-methyl-2,5′-dioxo-5′,6′-dihydrospiro[indoline-3,4′-pyrano-[3,2-*c*]quinolone]-3′-carbonitrile (**3e**) was distinguished. According to elemental analysis and mass spectrometry, compound **3e** has the gross formula $C_{21}H_{14}N_4O_3$, resulting from combination of one molecule of *N*-methylquinoline-2,4-dione (**1e**) with one molecule of **2**. Our first impression was that the reaction might give either **3e**, **4**, or **5** (Fig. 6). NMR data appear in Table 2.

The ^{13}C spectrum has 21 lines, consistent with **3e** but excluding structure **4**; 18 are in the normal sp^2 region between $\delta = 100$–160 ppm. Whereas the proposed structure of **5** was ruled out on the basis of 2D-NMR. The nitrogen atom of **3e** appeared at $\delta_N = 136.3$ ppm and gives HSQC correlation with the ^{1}H broadened singlet at $\delta = 10.54$ ppm. The former two signals are assigned as N-1 and the attached proton H-1 also gives HMBC correlation with the carbonyl carbon at 177.81 ppm, which is assigned as C-2. The sp^3 carbon at 48.15 ppm, assigned as the spiro carbon C-3,4′. In addition, C-7a gives HMBC correlation with a proton triplet at 7.18 ppm, assigned as H-6; this is another three-bond correlation, and the attached carbon appears at 128.28 ppm. The nitrogen at 140.50 ppm gives HMBC correlation with an aromatic doublet at 7.59 ppm, and a methyl singlet at 3.49 ppm. This nitrogen is assigned as N-6′ and the methyl singlet as H-6′b; the

Scheme 1



1a-1f **2** **3a-3f** (85-92%)

3a (85%), **3b** (92%), **3c** (90%), **3d** (88%), **3e** (87%), **3f** (86%)

1,3: a, $R^1 = R^2 = H$; **b**, $R^1 = H$, $R^2 = Cl$; **c**, $R^1 = H$, $R^2 = Br$; **d**, $R^1 = H$, $R^2 = Me$; **e**, $R^1 = Me$, $R^2 = H$; **f**, $R^1 = Et$, $R^2 = H$

Table 1 NMR assignments of compound **3a**

^{1}H NMR	^{1}H-^{1}H COSY	Assig.
11.75 (bs, 1H)		NH-6′
10.53 (bs, 1H)		NH-1
7.96 (d, J = 7.8 Hz, 1H)	7.63	H-10′
7.63 (ddd, J = 8.3, 7.2, 1.1 Hz, 1H)	7.96, 7.36	H-8′
7.46 (bs, 2H)		NH_2
7.36 (d, J = 8.1 Hz, 1H)	7.63	H-7′
7.34 (dd, J = 7.5, 7.5 Hz, 1H)	7.63	H-9′
7.19 (ddd, J = 7.6, 7.6, 0.7 Hz, 1H)	7.04, 6.90, 6.84	H-6
7.04 (d, J = 7.3 Hz, 1H)	7.19, 6.90, 6.84	H-4
6.90 (dd, J = 7.5, 7.4 Hz, 1H)	7.19, 7.04, 6.84	H-5
6.84 (d, J = 7.7 Hz, 1H)	7.19, 7.04, 6.90	H-7

^{15}N NMR	HSQC	HMBC	Assig.
146.2	11.75	7.36	N-6′
136.3	10.54	6.84	N-1
75.3	7.46		NH_2

^{13}C NMR	HSQC	HMBC	Assig.
177.83	10.54		C-2
159.40, 158.94	11.75, 7.48		C-5′,2′
152.39	11.75, 7.96, 7.48, 7.36		C-10′a
142.37	10.54, 7.19, 7.04, 6.90, 6.84		C-7a
137.82	11.75, 7.96, 7.63, 7.34		C-6′a
134.31	10.54, 7.19, 6.90, 6.84		C-3a
131.77	7.63	7.96	C-8′
128.28	7.19	7.04, 6.90	C-6
123.46	7.04	7.19	C-4
122.16	7.34, 7.63, 7.36		C-9′
121.91	6.90	6.84	C-5
121.68	7.96	7.63	C-10′
117.48			CN
115.37	7.36	11.75, 7.34	C-7′
111.55	11.75, 7.63, 7.36, 7.34		C-10′b
109.22	6.84	7.18, 7.04, 6.90	C-7
106.99	11.75		C-4′a
57.18	7.48		C-3′
47.75	11.75, 10.54, 7.04, 6.84		C-3,4′

carbon attached to H-6′b appears at 29.19 ppm, and is assigned as C-6′b. The nitrogen at 75.20 ppm is assigned as NH_2. The carbon at 57.22 ppm gives HMBC correlation with NH_2, and is assigned as C-3′; its upfield shift is attributed to the observed trends in δ values for C-atoms in push–pull alkenes [44, 45]. The carbon C-10′b appears at 112.27 ppm, and gives HMBC correlation with H-7′ and NH_2. The remaining carbons appear at 117.43 and 106.48 ppm, and must be CN and C-4′a; based on chemical shifts, the downfield of the two is assigned as the nitrile carbon-CN and the upfield carbon as C-4′a. The rest of the assignments in the two benzene rings follow straightforwardly from the correlations in Table 2.

The spectra of the *N*-ethyl compound **3f** are essentially identical to those of **3e**; because spiro carbon C-14 is a stereogenic center, protons of H-101 are diastereotopic (Fig. 7) [46], and the *N*-ethyl group appears as an ABX_3 system. The structure assignment of **3f** is unambiguously

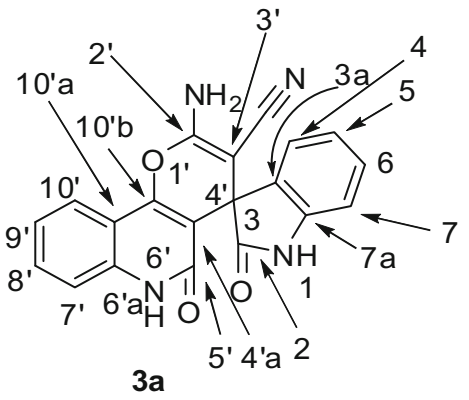


Fig. 1 Distinctive carbons and hydrogens for compound **3a**

confirmed by an X-ray crystal structure; the crystal contains one equivalent of DMF, the recrystallization solvent (Fig. 7).

We propose the mechanism shown in Scheme 2. Conjugate addition of **1** to **2**, catalyzed by base, would give intermediate **B**. Cyclization of **B** would then occur to give intermediate **C** and, after proton transfer, finally give products **3a**–**3f** (Scheme 2).

Most indicative is the ring conformation in crystals of compounds **3a**–**3d** and **3f** are distorted under the effect of intermolecular interactions, as is evidenced by short intermolecular contacts. The complexes are stabilized by intermolecular N–H···O and C–H···O hydrogen bonds between the hydrogen atoms situated inside the cavity of

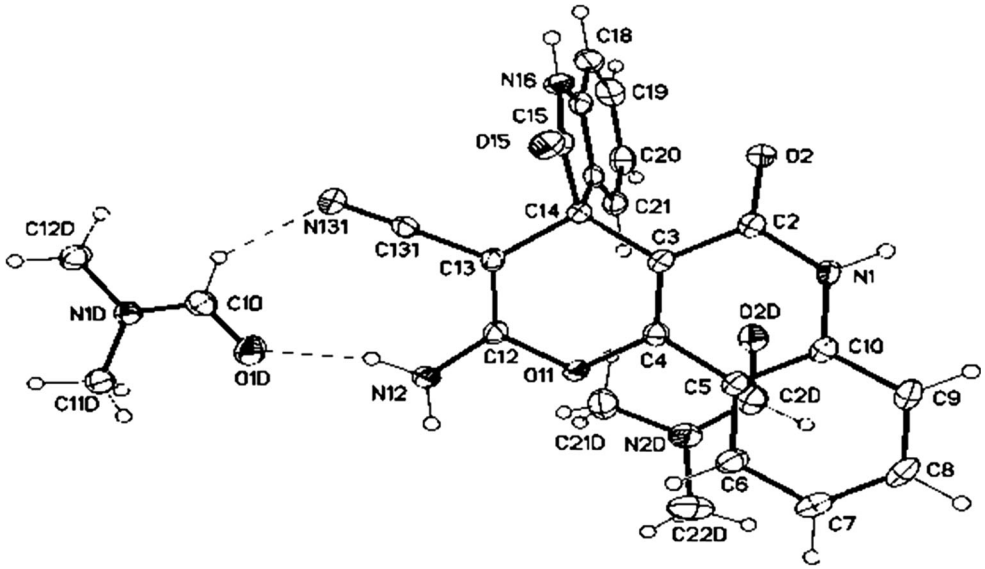


Fig. 2 Molecular structure of **3a** DMF. Displacement parameters are drawn at 50% probability level

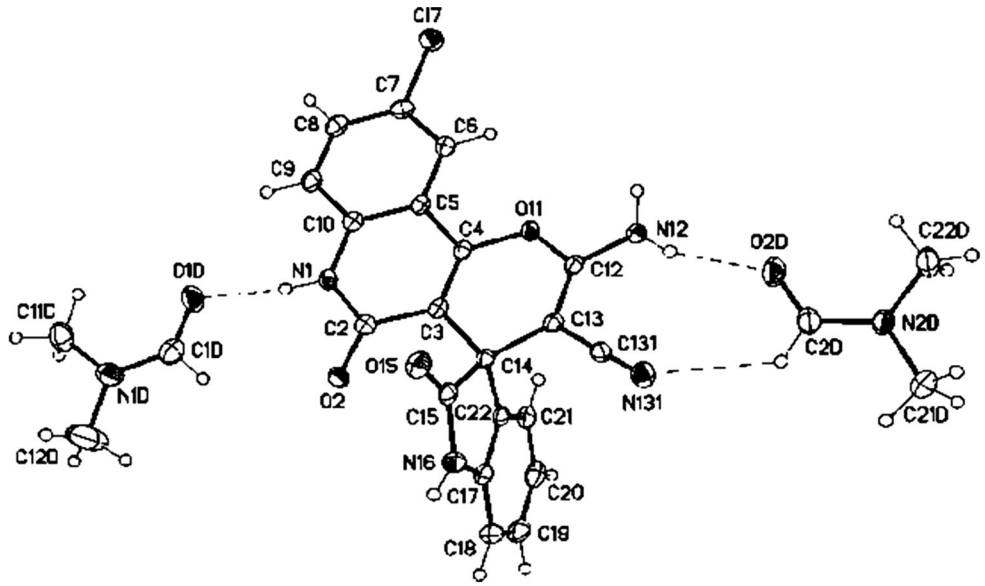


Fig. 3 Molecular structure of **3b** 2DMF. Displacement parameters are drawn at 50% probability level

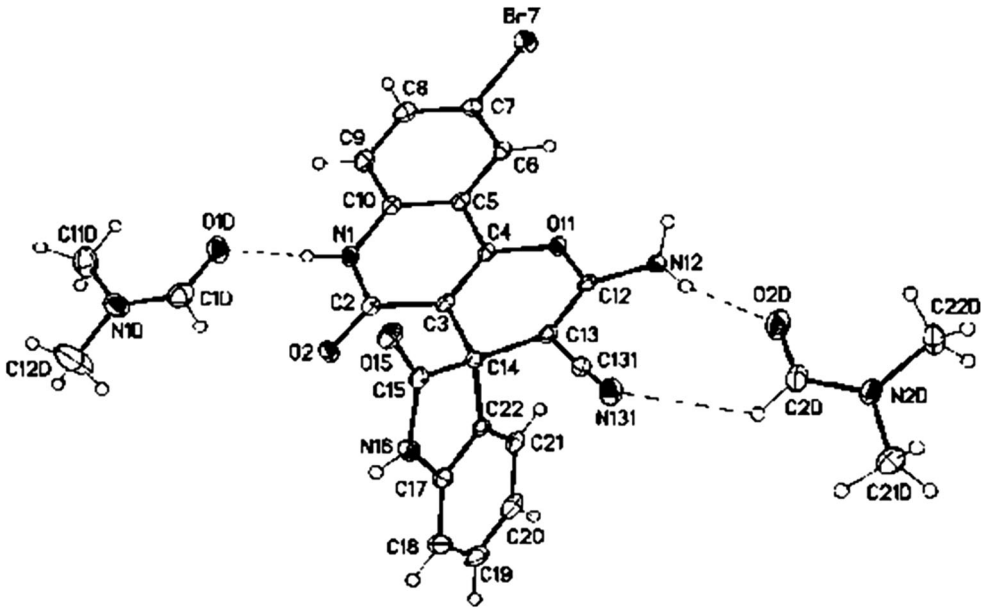


Fig. 4 Molecular structure of **3c** 2DMF. Displacement parameters are drawn at 50% probability level

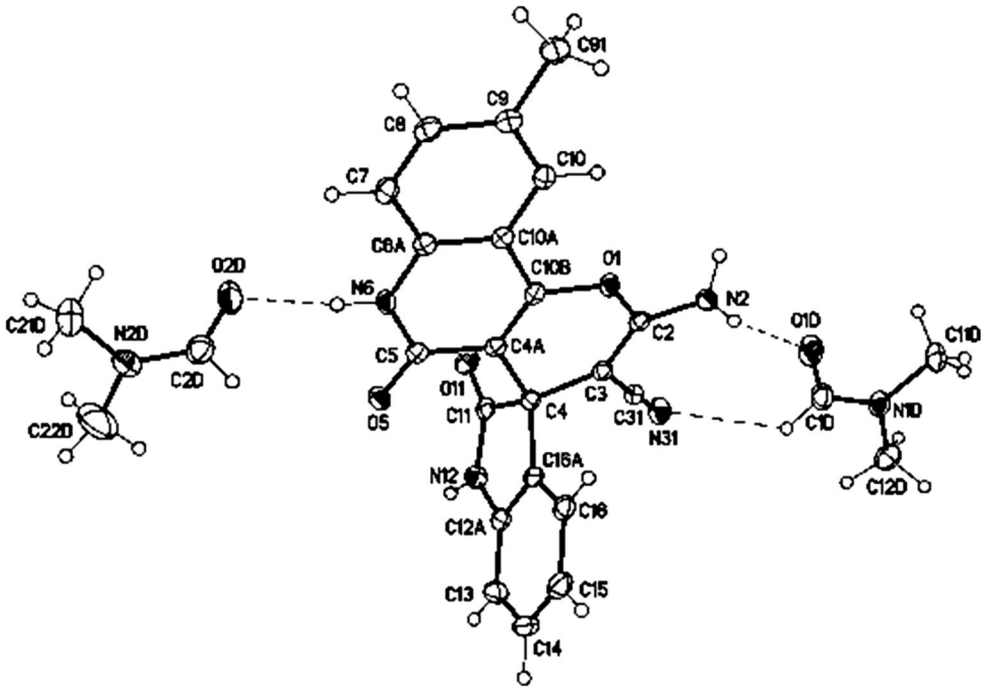


Fig. 5 Molecular structure of **3d** 2DMF. Displacement parameters are drawn at 50% probability level

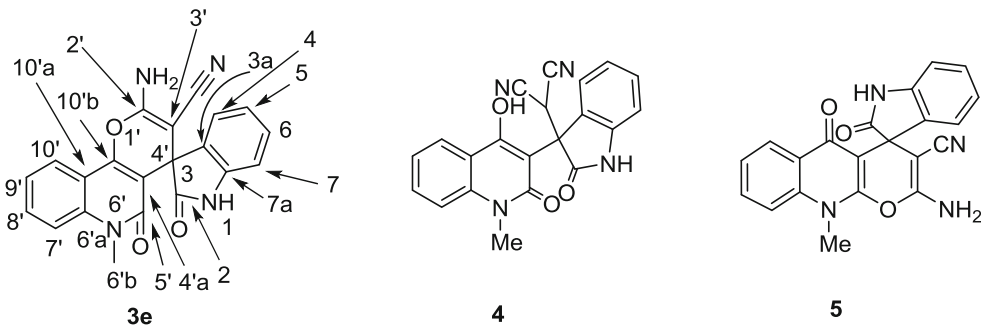


Fig. 6 Alternative expected structures **4** and **5** of compound **3e**

Table 2 NMR assignment of compound **3e**

^{1}H NMR	^{1}H-^{1}H COSY	Assig.
10.54 (bs, 1H)		NH-1
8.07 (d, $J = 8.0$ Hz, 1H) 7.76		H-10′
7.76 (dt, $J_t = 7.3$, $J_d = 1.1$ Hz, 1H)	8.07, 7.59, 7.45	H-8′
7.59 (d, $J = 8.6$ Hz, 1H)	7.76, 7.45	H-7′
7.48 (bs, 2H)		NH_2
7.45 (t, $J = 7.7$ Hz, 1H)	7.76	H-9′
7.18 (t, $J = 7.6$ Hz, 1H)	7.02, 6.88, 6.85	H-6
7.02 (d, $J = 7.2$ Hz, 1H)	6.88, 6.85	H-4
6.88 (t, $J = 7.5$ Hz, 1H)	7.18, 7.02	H-5
6.85 (d, $J = 7.8$ Hz, 1H)	7.18, 7.02	H-7
3.49 (s, 3H)		CH_3

^{15}N NMR	HSQC	HMBC	Assig.
140.5	7.59, 3.49		N-6′
136.3	10.54	6.85	N-1
75.2	7.48		NH_2

^{13}C NMR	HSQC	HMBC	Assig.
177.81	10.54		C-2
158.87, 158.72		7.48, 3.49	C-5′,2′
151.46		8.07, 7.59	C-10′a
142.48		10.54, 7.18, 7.02, 6.85	C-7a
138.64		8.07, 7.76, 3.49	C-6′a
134.25		10.54 ,6.88, 6.85	C-3a
132.23	7.76	8.07, 7.59	C-8′
128.28	7.18	7.02, 6.88	C-6
123.40	7.02	7.18	C-4
122.41, 122.36	8.07, 7.45	7.76, 7.59	C-9′,10′
121.66	6.88	6.85	C-5
117.43			CN
115.03	7.59	3.49	C-7′
112.27		7.59, 7.48	C-10′b
109.18	6.85	6.88	C-7
106.48			C-4′a
57.22		7.48	C-3′
48.15		10.54, 7.02, 6.88, 6.85	C-3,4′
29.19	3.94	CH_3	

the macrocycle, the oxygen and nitrogen atoms of the dimethylformamide (DMF) and water molecules.

Conclusion

Reaction of 2,4-quinolinediones with isatinemalononitrile yields spiro-compounds in good yields; structures were established by solution-phase spectroscopy and X-ray crystallographic analysis.

Experimental

NMR spectra were measured in DMSO-d_6 on a Bruker AV-400 spectrometer (Bruker BioSpin Corp., Billerica, MA, USA) (400.13 MHz for ^{1}H, 100.13 MHz for ^{13}C, and 40.55 MHz for ^{15}N) at Florida Institute of Technology, USA. The ^{1}H and ^{13}C chemical shifts are given relative to internal standard TMS; ^{15}N shifts are reported versus external liquid ammonia. For preparative thin layer chromatography (PLC), glass plates (20 × 48 cm) were

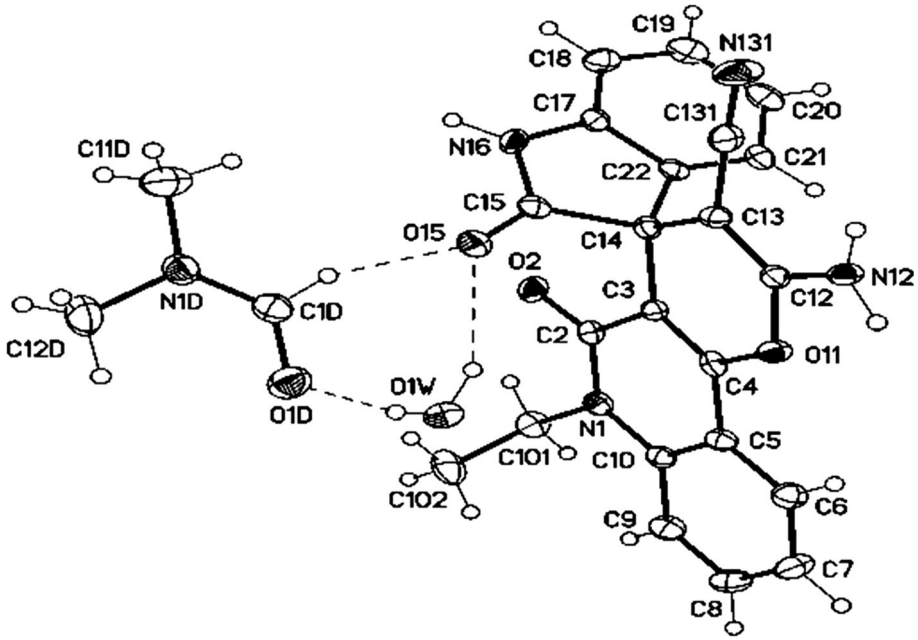
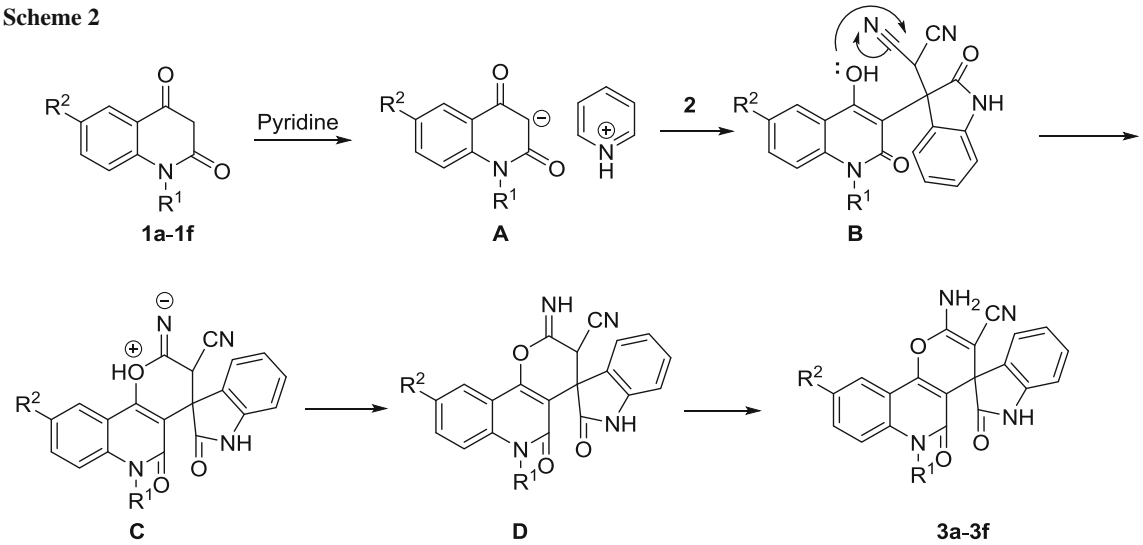


Fig. 7 Molecular structure of **3f** DMF. Displacement parameters are drawn at 50% probability level

Scheme 2



covered with a slurry of silica gel Merck PF254 and air dried and developed using the solvents listed. Zones were detected by quenching of indicator fluorescence upon exposure to 254 nm UV light. Elemental analyses were carried in the National Research Center, Dokki, Cairo, Egypt. Mass spectra were recorded on a Varian MAT 312 instrument in EI mode (70 eV), at the Karlsruhe Institut für Technologie (KIT), Institute of Organic Chemistry, Karlsruhe, Germany. IR spectra using KBr pellets, were run on a FT-IR (Bruker), Minia University, El-Minia, Egypt. Quinoline-2,4-diones **1a**–**1f** were prepared according to the literature [47].

X-ray crystal structure determination

The single-crystal X-ray diffraction study were carried out on a Bruker D8 Venture diffractometer with Photon100 detector at 123(2) K using Cu-Kα radiation (**3a**, **3b**, **3d**, **3f**, $\lambda = 1.54178$ Å) or Mo-Kα radiation (**3c**, $\lambda = 0.71073$ Å). Direct Methods (SHELXS-97) [48] or dual space methods (**3d**) [49] were used for structure solution and refinement was carried out using SHELXL-2014 (full-matrix least-squares on F^2) [49]. Hydrogen atoms were localized by difference electron density determination and refined using a riding model (H(N) and H(O) free. Semi-empirical

absorption corrections were applied. For **3a**, **3c**, and **3d** extinction corrections were applied.

CCDC-1519994 (**3a**), CCDC-1519995 (**3b**), CCDC-1519996 (**3c**), CCDC-1574003 (**3d**) and CCDC-1519997 (**3f**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

General procedure for the reaction of quinoline-2,4-diones 1a–1f with 2

A 100 cm^3 round-bottom flask was flame-dried, a mixture of **1a–1f** (1 mmol), **2** (1 mmol), and 20 cm^3 dry pyridine was refluxed for 8–10 h with stirring (the reaction was followed by TLC analysis). After the reaction's completion, solvent was then removed under vacuum and the residue was separated. The solid residue undergoes recrystallization from the stated solvents to give pure crystals of spiro-compounds **3a–3f**.

2′-Amino-2,5′-dioxo-5′,6′-dihydrospiro[indoline-3,4′-pyrano-[3,2-c]quinolone]-3′-carbonitrile (**3a**, $C_{20}H_{12}N_4O_3$)
Colorless crystals (DMF); yield 303 mg (85%), m.p.: 298–300 °C; NMR (DMSO-d_6): see Table 1; IR (KBr): $\bar{\nu}$ = 3372–3207 (NH, NH_2), 3099 (Ar–H), 2205 (CN), 1725, 1672, 1642 (C=O), 1600, 1596 (Ar–C=N, Ar–C=C) cm^{-1}; MS (FAB, 70 eV): *m/z* = 356 (M^+, 100).

Crystal structure data for **3a**: colourless crystals, $C_{20}H_{12}N_4O_3{\cdot}2(C_3H_7NO)$, M_r = 502.53, crystal size 0.16 × 0.10 × 0.08 mm, monoclinic, space group $P2_1/c$ (No. 14), a = 10.8078(3) Å, b = 21.4185(6) Å, c = 11.0025(3) Å, β = 106.635(1)°, V = 2440.34(12) $Å^3$, Z = 4, ρ = 1.368 Mg m^{-3}, μ(Cu-K_α) = 0.805 mm^{-1}, $F(000)$ = 1056, $2\theta_{max}$ = 144.4°, 26,760 reflections, of which 4805 were independent (R_{int} = 0.042), 351 parameters, 4 restraints, R_1 = 0.038 (for 4182 $I > 2\sigma(I)$), wR_2 = 0.097 (all data), S = 1.06, largest diff. peak/-hole = 0.297/− 0.206 e $Å^{-3}$.

2′-Amino-9′-chloro-2,5′-dioxo-5′,6′-dihydrospiro[indoline-3,4′-pyrano[3,2-c]quinolone]-3′-carbonitrile
(**3b**, $C_{20}H_{11}ClN_4O_3$)
Colorless crystals (DMF/EtOH); yield 360 mg (92%), m.p.: 320–322 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.88 (bs, 1H, NH-6′), 10.55 (bs, 1H, NH-1), 8.00 (d, J = 2.3 Hz, 1H, H-10′), 7.68 (dd, J = 8.8, 2.4 Hz, 1H, H-8′), 7.47 (bs, 2H, NH_2), 7.37 (d, J = 8.8 Hz, 1H, H-7′), 7.19 (ddd, J = 7.6, 7.6, 0.7 Hz, 1H, H-6), 7.05 (d, J = 7.3 Hz, 1H, H-4), 6.90 (dd, J = 7.4, 7.4 Hz, 1H, H-5), 6.83 (d, J = 7.7 Hz, 1H, H-7) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 177.58 (C-2), 159.18, 158.77 (C-5′,2′), 151.44 (C-10′a), 142.33 (C-7a), 136.55 (C-6′a), 134.06 (C-3a), 131.71 (C-8′), 128.38 (C-6), 126.31 (C-9′), 123.56 (C-4), 121.71 (C-5), 121.23 (C-10′), 117.48, 117.30 (CN,C-7′), 111.55 (C-10′b), 109.24 (C-7), 107.98 (C-4′a), 57.09 (C-3′), 47.74 (C-3,4′) ppm; ^{15}N NMR (40 MHz, DMSO-d_6): δ = 146.0 (N-6′), 136.2 (N-1), 74.8 (NH_2) ppm; IR (KBr): $\bar{\nu}$ = 3350–3196 (NH, NH_2), 3031 (Ar–CH), 2928 (Ali-CH), 2193 (CN), 1716, 1669, 1654 (C=O), 1605, 1593 (Ar–C=N, Ar–C=C) cm^{-1}; MS (FAB, 70 eV): *m/z* = 391 ($[M + 1]^+$, 28), 390 (M^+, 58).

Crystal structure data for **3b**: colourless crystals, $C_{20}H_{11}ClN_4O_3{\cdot}2(C_3H_7NO)$, M_r = 536.97, crystal size 0.20 × 0.16 × 0.10 mm, monoclinic, space group $P2_1/c$ (No. 14), a = 11.0744(4) Å, b = 21.3368(8) Å, c = 11.1215(4) Å, β = 107.884(1)°, V = 2500.94(16) $Å^3$, Z = 4, ρ = 1.426 Mg m^{-3}, μ(Cu-K_α) = 1.784 mm^{-1}, $F(000)$ = 1120, $2\theta_{max}$ = 144.2°, 21,016 reflections, of which 4915 were independent (R_{int} = 0.027), 359 parameters, 4 restraints, R_1 = 0.036 (for 4445 $I > 2\sigma(I)$), wR_2 = 0.097 (all data), S = 1.03, largest diff. peak/-hole = 0.320/− 0.290 e $Å^{-3}$.

2′-Amino-9′-bromo-2,5′-dioxo-5′,6′-dihydrospiro[indoline-3,4′-pyrano[3,2-c]quinolone]-3′-carbonitrile
(**3c**, $C_{20}H_{11}BrN_4O_3$)
Colorless crystals (DMF/MeOH); yield 390 mg (90%), m.p.: > 360 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.87 (bs, 1H, NH-6′), 10.55 (bs, 1H, NH-1), 8.14 (d, J = 2.2 Hz, 1H, H-10′), 7.79 (dd, J = 8.8, 2.2 Hz, 1H, H-8′), 7.48 (bs, 2H, NH_2), 7.31 (d, J = 8.8 Hz, 1H, H-7′), 7.18 (ddd, J = 7.6, 7.6, 0.9 Hz, 1H, H-6), 7.05 (d, J = 7.2 Hz, 1H, H-4), 6.89 (dd, J = 7.5, 7.5 Hz, 1H, H-5), 6.83 (d, J = 7.7, 1H, H-7) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 177.59 (C-2), 159.17, 158.77 (C-5′,2′), 151.36 (C-10′a), 142.33 (C-7a), 136.86 (C-6′a), 134.36 (C-8′), 134.07 (C-3a), 128.38 (C-6), 124.22 (C-10′), 123.56 (C-4), 121.71 (C-5), 117.62 (C-7′), 117.31 (CN), 114.01 (C-9′), 113.24 (C-10′b), 109.24 (C-7), 107.98 (C-3a), 57.09 (C-3′), 47.74 (C-3,4′) ppm; ^{15}N NMR (40 MHz, DMSO-d_6): δ = 146.2 (N-6), 136.4 (N-4c), 75.1 (NH_2) ppm; IR (KBr): $\bar{\nu}$ = 3365–3195 (NH, NH_2), 3044 (Ar–CH), 2930 (Ali-CH), 2195 (CN), 1700, 1671, 1635 (C=O), 1605, 1589 (Ar–C=N, Ar–C=C) cm^{-1}; MS (FAB, 70 eV): *m/z* = 435 ($[M + 1]^+$, 28), 434 (M^+, 56).

Crystal structure data for **3c**: colourless crystals, $C_{20}H_{11}BrN_4O_3{\cdot}2(C_3H_7NO)$, M_r = 581.43, crystal size 0.25 × 0.20 × 0.15 mm, monoclinic, space group $P2_1/c$ (No. 14), a = 11.0650(5) Å, b = 21.4404(11) Å, c = 11.2361(5) Å, β = 108.179(2)°, V = 2532.6(2) $Å^3$, Z = 4, ρ = 1.525 Mg m^{-3}, μ(Mo-K_α) = 1.673 mm^{-1}, $F(000)$ = 1192, $2\theta_{max}$ = 55.2°, 39,390 reflections, of which 5834 were independent (R_{int} = 0.024), 360 parameters, 4 restraints, R_1 = 0.026 (for 5290 $I > 2\sigma(I)$), wR_2 = 0.064 (all data), S = 1.05, largest diff. peak/-hole = 0.483/− 0.572 e $Å^{-3}$.

2′-Amino-9′-methyl-2,5′-dioxo-5′,6′-dihydrospiro[indoline-3,4′-pyrano[3,2-c]quinolone]-3′-carbonitrile
(**3d**, $C_{21}H_{14}N_4O_3$)
Colorless crystals (DMF); yield 325 mg (88%), m.p.: 340–342 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.83 (bs, 1H, NH-6′), 10.69 (bs, 1H, NH-1), 7.94 (s, 1H, H-10′), 7.62 (d, J = 8.4 Hz, 1H, H-8′), 7.61 (bs, 2H, NH_2), 7.43 (d, J = 8.4 Hz, 1H, H-7′), 7.35 (t, J = 7.6 Hz, 1H, H-6), 7.18 (d, J = 7.3 Hz, 1H, H-4), 7.06 (t, J = 7.4 Hz, 1H, H-5), 7.00 (d, J = 7.7 Hz, 1H, H-7), 2.59 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 177.86 (C-2), 159.26, 158.96 (C-5′,2′), 152.23 (C-10′a), 142.37 (C-7a), 135.90 (C-6′a), 134.39 (C-3a), 132.97 (C-8′), 131.27 (C-9′), 128.23 (C-6), 123.38 (C-4), 121.64 (C-10′), 121.29 (C-5), 117.47 (CN), 115.30 (C-7′), 111.45 (C-10′b), 109.19 (C-7), 106.94 (C-4′a), 57.19 (C-3′), 47.77 (C-3,4′), 20.65 (CH_3) ppm; ^{15}N NMR (40 MHz, DMSO-d_6): δ = 145.5 (N-6′), 136.2 (N-1), 74.8 (NH_2) ppm; IR (KBr): $\bar{\nu}$ = 3370–3190 (NH, NH_2), 3033 (Ar–CH), 2922 (Ali-CH), 2198 (CN), 1705, 1670, 1638 (C=O), 1610, 1587 (Ar–C=N, Ar–C=C) cm^{-1}; MS (FAB, 70 eV): *m/z* = 370 (M^+, 100).

Crystal structure data for **3d**: colourless crystals, $C_{21}H_{14}N_4O_3{\cdot}2(C_3H_7NO)$, M_r = 516.55, crystal size 0.18 × 0.06 × 0.03 mm, monoclinic, space group $P2_1/c$ (No. 14), a = 11.0806(5) Å, b = 21.3920(9) Å, c = 11.1076(5) Å, β = 107.616(2)°, V = 2509.44(19) Å^3, Z = 4, ρ = 1.367 Mg m^{-3}, μ(Cu-K$_\alpha$) = 0.798 mm^{-1}, $F(000)$ = 1088, $2\theta_{max}$ = 144.0°, 23,702 reflections, of which 4913 were independent (R_{int} = 0.041), 361 parameters, R_1 = 0.039 (for 4146 $I > 2\sigma(I)$), wR_2 = 0.100 (all data), S = 1.03, largest diff. peak/hole = 0.275/− 0.226 e Å^{-3}.

2′-Amino-6′-methyl-2,5′-dioxo-5′,6′-dihydrospiro[indoline-3,4′-pyrano[3,2-c]quinolone]-3′-carbonitrile
(**3e**, $C_{21}H_{14}N_4O_3$)
Colorless crystals (DMF); yield 322 mg (87%), m.p.: 310–312 °C; NMR (DMSO-d_6): see Table 2; IR (KBr): $\bar{\nu}$ = 3359–3166 (NH, NH_2), 2193 (CN), 1711, 1672, 1645 (C=O), 1626, 1598 (Ar–C=N, Ar–C=C) cm^{-1}; MS (FAB, 70 eV): *m/z* = 370 (M^+, 60).

2′-Amino-6′-ethyl-2,5′-dioxo-5′,6′-dihydrospiro[indoline-3,4′-pyrano[3,2-c]quinolone]-3′-carbonitrile
(**3f**, $C_{22}H_{16}N_4O_3$)
Colorless crystals (DMF/EtOH); yield 330 mg (86%), m.p.: 330–332 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.53 (bs, 1H, NH-1), 8.09 (dd, J = 8.0, 1.2 Hz, 1H, H-10′), 7.76 (dt, J_t = 7.2 Hz, J_d = 1.3 Hz, 1H, H-8′), 7.64 (d, J = 8.6 Hz, 1H, H-7′), 7.48 (bs, 2H, NH_2), 7.43 (t, J = 7.6 Hz, 1H, H-9′), 7.18 (dt, J_t = 7.6 Hz, J_d = 0.9 Hz, 1H, H-6), 7.03 (d, J = 7.2 Hz, 1H, H-4), 6.88 (t, J = 7.5 Hz, 1H, H-5), 6.85 (d, J = 7.8 Hz, 1H, H-7), 4.14 (ABX$_3$, J_{AB} = 13.3 Hz, J_{AX} = 7.0 Hz, 1H, CH_2CH_3), 4.11 (ABX$_3$, J_{AB} = 13.3 Hz, J_{BX} = 7.0 Hz, 1H, CH_2CH_3), 1.08 (ABX$_3$, $J_{AX} = J_{BX}$ = 7.0 Hz, 3H, CH_2CH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 177.84 (C-2), 158.88, 158.33 (C-5′,2′), 151.49 (C-10′a), 142.46 (C-7a), 137.58 (C-6′a), 134.27 (C-3a), 132.31 (C-8′), 128.29 (C-6), 123.37 (C-4), 122.66 (C-10′), 122.27 (C-9′), 121.70 (C-5), 117.44 (CN), 114.73 (C-7′), 112.49 (C-10′b), 109.21 (C-7), 106.42 (C-4′a), 57.22 (C-3′), 48.13 (C-3,4′), 36.83 (N-CH_2CH$_3$), 12.62 (N-CH$_2$$CH_3$) ppm; ^{15}N NMR (40 MHz, DMSO-d_6): δ = 154.3 (N-6′), 136.5 (N-1), 75.1 (NH_2) ppm; IR (KBr): $\bar{\nu}$ = 3360–3192 (NH_2, NH), 3106 (Ar–CH), 2967 (Ali-CH), 2205 (CN), 1725, 1672, 1642 (C=O), 1600, 1578 (Ar–C=N, Ar–C=C) cm^{-1}; MS (FAB, 70 eV): *m/z* = 384 (M^+, 100).

Crystal structure data for **3f**: colourless crystals, $C_{22}H_{16}N_4O_3{\cdot}C_3H_7NO{\cdot}H_2O$, M_r = 475.50, crystal size 0.16 × 0.10 × 0.04 mm, triclinic, space group P-1 (No. 2), a = 9.6532(5) Å, b = 11.3165(6) Å, c = 12.6497(6) Å, α = 110.480(3)°, β = 102.514(3)°, γ = 107.481(3)°, V = 1151.89(11) Å^3, Z = 2, ρ = 1.371 Mg m^{-3}, μ(Cu-K$_\alpha$) = 0.807 mm^{-1}, $F(000)$ = 500, $2\theta_{max}$ = 136.4°, 11,728 reflections, of which 4141 were independent (R_{int} = 0.037), 333 parameters, 5 restraints, R_1 = 0.055 (for 3170 $I > 2\sigma(I)$), wR_2 = 0.155 (all data), S = 1.05, largest diff. peak/hole = 0.354/− 0.254 e Å^{-3}.

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