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ORIGINAL PAPER

One-pot synthesis of 2,3-bis-(4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)succinates and arylmethylene-bis-3,3′-quinoline-2-ones

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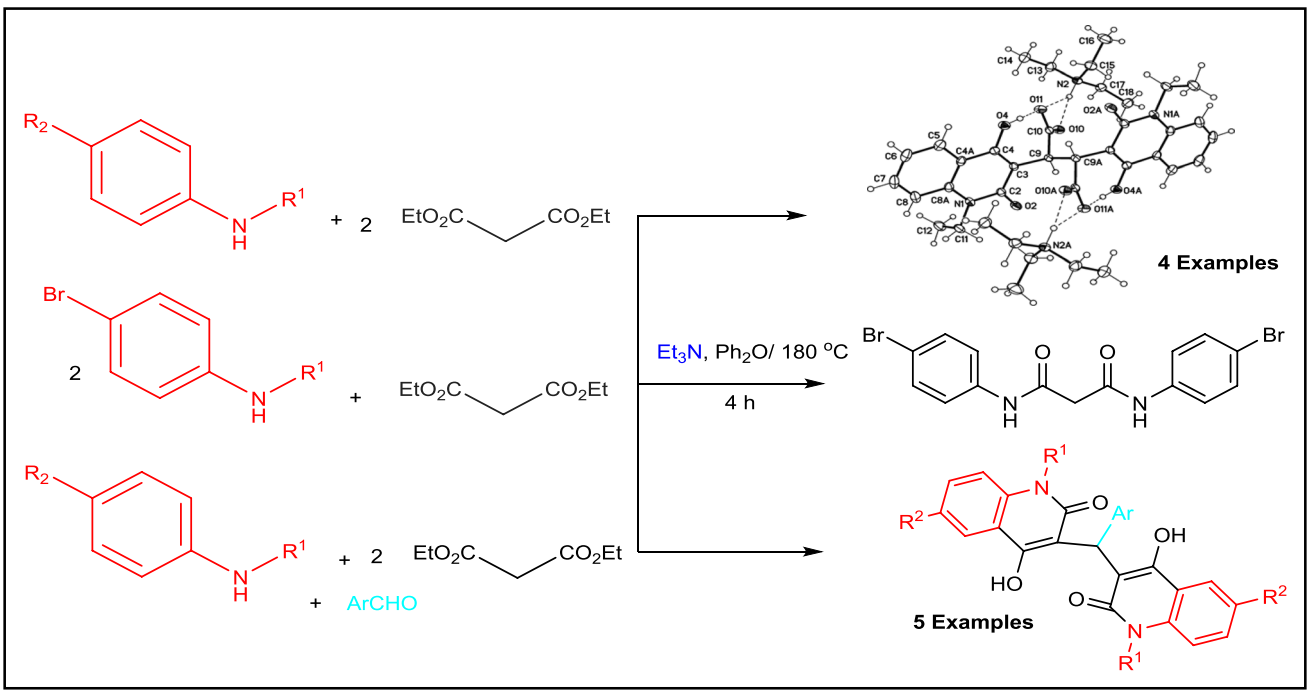
Abstract

In this investigation an efficient synthesis of 2,3-bis-(4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)succinic acid derivatives was achieved by one-pot reaction of one equivalent of aromatic amines with two equivalents of diethyl malonate in diphenyl ether and catalyzed with triethylamine. In case of applying the previous condition with aromatic amines and diethyl malonate in a ratio of 2:1, no quinolone structure was obtained, whereas N^1,N^3-bis(4-bromophenyl)malonamide, as an example, was obtained in 95% yield. Under the same previous condition, arylmethylene-bis-3,3′-quinoline-2-ones were in one pot synthesized via the reaction of equal equivalents of aromatic amines and diethyl malonate together with half equivalent of the corresponding aromatic aldehydes. The structure of the obtained compounds was proved by IR, NMR and mass spectra and X-ray structure analyses.

Graphical abstract



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Keywords Bis-(quinolin-3-yl)succinates · N^1,N^3-bis(4-bromophenyl)malonamide arylmethylene-bis-3,3′-quinoline-2-ones · One-pot synthesis · X-ray

Introduction

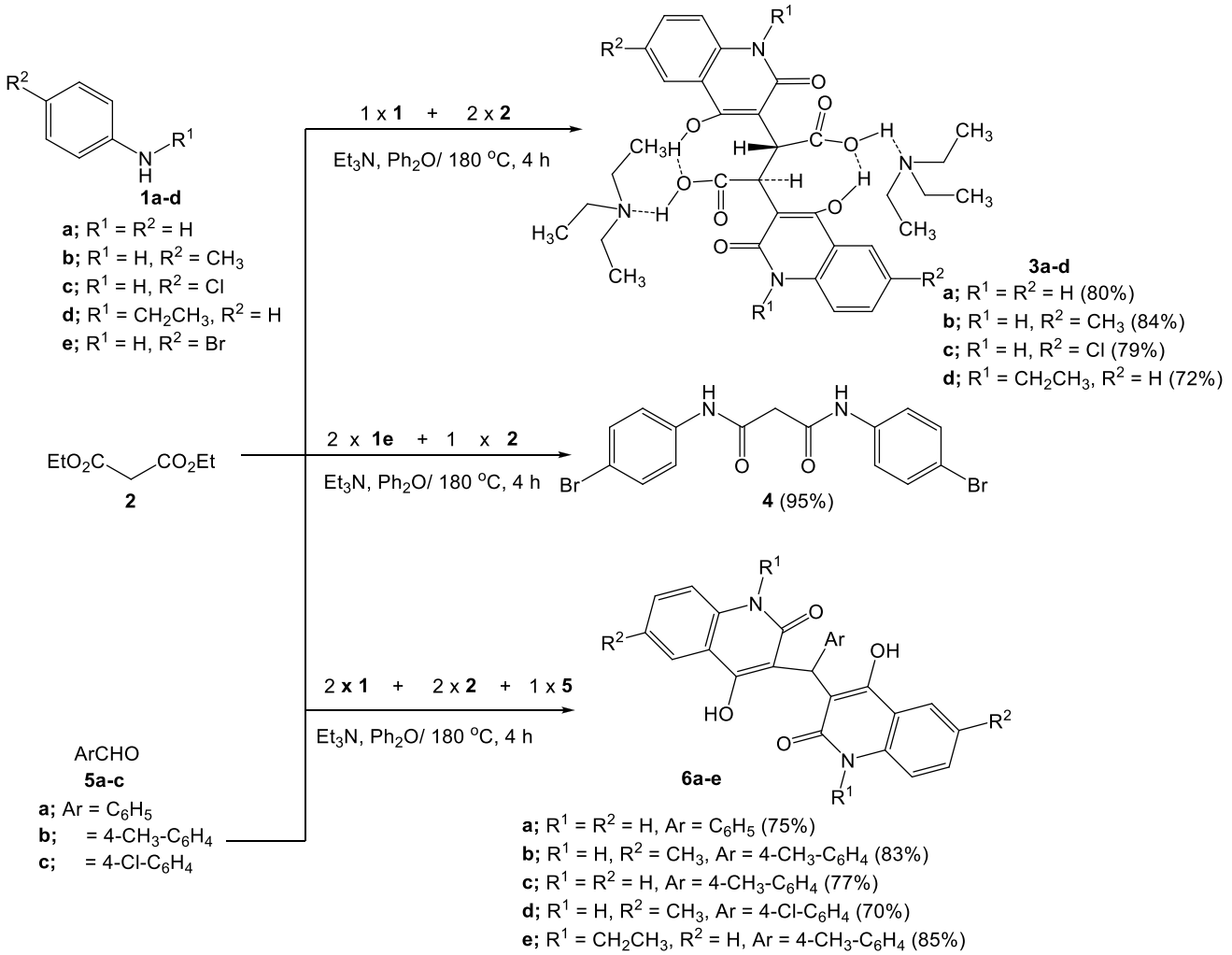
2-Quinolones (Chen et al. 2001) have showed considerable interest because of their pharmacological importance (Abass et al. 2015) and various biological activities (Abass and Mostafa 2005). Various quinolones are described to have antimicrobial (Al-Trawneh et al. 2010; Eswaran et al. 2010), antifungal (Musiol et al. 2006), enzyme inhibitory (Slater and Cerami 1992), anti-HIV (Ahmed et al. 2010) , anti-oxidant (Sankaran et al. 2010) and cytotoxic activities (Ma et al. 2004). The quinolones are also occurring in natural products (Junichiro et al. 2012), mainly in alkaloids (Michael 2005). As for example, quinine is a quinoline-based alkaloid structure isolated from the bark of *cinchona* tree (Igarashi and Kobayashi 2005) and is used for the treatment of *Malaria*. Luotonin A (Cagir et al. 2003) is a cytotoxic alkaloid as a cytotoxic alkaloid drug, which is used in treatment of rheumatism and inflammation. Quinarcine (Thi et al. 2008) drug is of an acridine-based alkaloid structure which has been used as an antimalarial agent. Kynurenic acid (Turski et al. 1988) is of quinolone structure that can be used for the normal metabolism of amino acids and reveals neuro active activity. Interestingly, antimalarial drugs consist of amino quinoline skeletons (primaquine) and are used for the treatment of *Malaria* (Turski et al. 1988).

Synthesis of bis-quinolones has recently attracted much attention due to prospective high biological and pharmaceutical activities (Tarushi et al. 2011). For example, functionalized 4,4′-bisquinolones were synthesized by microwave-assisted Pd(0)-catalyzed one-pot borylation/Suzuki cross-coupling reactions or via Ni(0)-mediated homocouplings of 4-chloroquinolin-2(1*H*)-one precursors (Hashim et al. 2006). Bis-conjugates of quinine with quinolone antibiotics and amino acid linkers retain in vitro antimalarial activity with IC_{50} values ranging from 12 to 207 µM, similar to quinine itself (Panda et al. 2012). Recently, we have synthesized spiro(indoline-3,4′-pyrano[3,2-*c*]quinoline)-3′-carbonitriles from reaction of quinoline-2,4-diones with 2-(2-oxo-1,2-dihydroindol-3-ylidene)malononitrile (Aly et al. 2018). We also reacted quinolinediones and diethyl acetylenedicarboxylate to give pyranoquinoline-4-carboxylates and (quinolin-3-yl)fumarates in good yields (El-Sheref et al. 2018). Considering the importance of the interesting chemical behavior of quinolones, and in view of the promising aspects and making a further step forward, we report herein on the application of the one-pot technique in synthesis of the title compounds.

Results and discussion

To our delight, mixing of one molar proportion of aromatic amines **1a–d** to two molar equivalents of diethyl malonate (**2**) in diphenyl ether catalyzed with few drops of triethylamine (Et_3N) and when the mixture was heated at 180 °C for 4 h, the reaction gave 2,3-bis-(4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)succinic acid.bis(triethylamine) derivatives **3a–d** in 79–84% yields (Scheme 1). The structures of the products were fully consistent with their ^{1}H NMR, ^{13}C NMR, IR and mass spectra, elemental analyses and X-ray structure analysis as well. We choose compound **3a**, as an example, to confirm the structures. According to elemental analysis, the compound **3a** would be in accordance to the molecular weight equals 638.75. In the mass spectrum of **3a**, the molecular peak is the base peak and corresponding to the molecular weight of *m/z* 436. One can then conclude the presence of the two molecules of Et_3N in its crystal lattice, which was not noticed in mass spectrum. The latter was confirmed by the NMR spectra of **3a**. The IR spectrum revealed bands at ν 3400, 3210, 1720 and 1680, corresponding to OH, NH, carbonyl-acid and 2-carbonyl-quinolone groups. Figure 1 illustrates the NMR spectroscopic data of compound **3a**, where the ^{1}H NMR spectrum indicates three singlets, each for the two protons at δ 14.10 (COOH), 13.20 (OH), and 11.80 (NH). A quartet resonated at δ 3.17 for the 12 CH_2 protons of the two triethylamine units, and a triplet at δ 1.30 for the 18 CH_3 protons of the same units (see the "Experimental"). The two adjacent methine protons were resonated in the ^{1}H NMR spectrum as a singlet at δ 3.72. The ^{13}C NMR spectrum confirmed the ^{1}H NMR spectral data by showing the carbonyl-acid and carbonyl-quinolone carbon signals at δ 164.8 and 160.1, respectively. The CH_2- and CH_3-Et_3N appeared at $\delta = 50.0$ and 13.7, whereas the ethano-carbons of succinic acid appeared at δ 38.2. In case of **3d**, the ^{1}H NMR spectral data revealed the presence of two molecules of Et_3N in its crystal lattice structure as a quartet at δ 3.20 for 18 protons and a triplet at δ 1.15 for 12 protons. Another two ethyl protons of *N*-1 for quinolone moiety appeared in the ^{1}H NMR spectrum as a quartet and triplet at δ 3.15 and 1.17, respectively ("Experimental" Section). The ^{1}H NMR spectrum showed also the two methine protons as a singlet at δ 3.70. The structure of **3d** was then totally proved by X-ray structure analysis (Fig. 2).

Since the structures of compounds **3a–d** involve two stereogenic centers, in principle two diastereoisomers should



Scheme 1 One-pot synthesis of 2,3-bis-(4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)succinates **3a–d**, N^1,N^3-bis(4-bromophenyl)malonamide (**4**) and arylmethylene-bis-3,3′-quinoline-2-ones **6a–e**

be obtained. One of these stereoisomers is the anti-form. Interestingly, the reaction proceeded to give only one diastereomers. Two types of hydrogen bonds were formed; one was held between the oxygen of the carboxylic-OH and the hydrogen atom of the hydroxyl group of 4-hydroxyquinolone. The other hydrogen bond was held between the nitrogen lone pair in triethylamine and the hydrogen atom of the free carboxylic-OH. Formation of such two types of hydrogen bonds would be expected to stabilize the anti-form structure of **3a–d** as shown in Scheme 1. The X-ray structure analysis confirmed the *meso* (*R*, *S*) configuration of compounds **3a–d**, as shown in Fig. 2.

It is well known that both ester enolates and carboxylic acid dianions can be used for oxidative homocoupling. The reaction mechanism can be explained as due to condensation between **1** and **2**, which would form 2-quinolone **8**. Subsequently, condensation between **8** and another molecule of **2** would give the fused α-pyranone **9** (Scheme 2). Addition of water to **9** would then give intermediate **10**, which was in equilibrium with its tautomer (Scheme 2). Finally, autoxidation of the α-ketonic acid **10** accompanied with elimination of CO_2 and rearrangement would then give salt **11**. Further oxidation of two molecules of **11** would produce target molecule **3** (Scheme 2). To ensure the reaction pathway, we also heat compound **9** in diphenyl ether at 180 °C for 3 h and successfully obtain **3**.

Interestingly, when we carried out the reaction between **1** and **2** in a molar ration of 2:1, we could not separate any quinolonoyl structure and we obtained malonamide **4** (Chattaway and Mason 1910; Vennerstrom and Holmes 1987) (Scheme 1). X-ray structure analysis of **4** is as shown in Fig. 3.

Inspired by the above results, we extended our studies to react aromatic amines **1a–d** with diethyl malonate (**2**) and aromatic aldehydes **5a–c** in a molar ratio of 2:2:1 and under the condition mentioned above (Scheme 1). We surprisingly

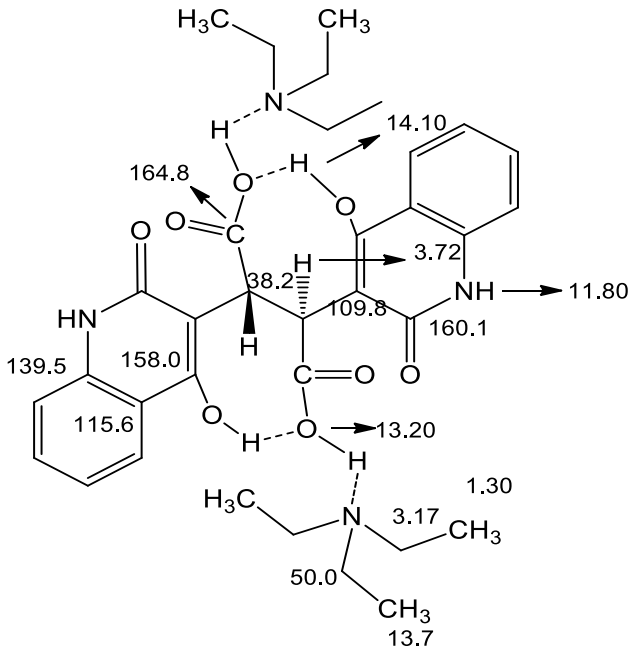


Fig. 1 NMR spectroscopic data some distinctive hydrogen protons and carbons of compound **3a**

obtained arylmethylene-bis-3,3′-quinoline-2-ones **6a–e** in good yields as shown in Scheme 1. Previously, another derivative of **6** (Bhat and Trivedi 2014) was obtained by reacting 4-hydroxy-*N*-methylquinolin-2(1*H*)-ones with benzaldehyde derivatives under solvent- and catalyst-free reaction conditions at 80 °C. The reactants underwent a cascade Knoevenagel–Michael reaction to yield other derivatives **6** in good yields (Bhat and Trivedi 2014). The main difference between our method and the previous method is that we prepared compounds **6** in one step in relatively good yields. Moreover, no literatures have discussed the regio-structure of **6** (Madhu et al. 2017), whether it is in *anti*- or *syn* form. To the best of our knowledge, NMR spectral data of **6a–e** derivatives have not reported yet. NMR spectral data of the product **6b** (Fig. 4), as an example, which was obtained from the reaction of 4-methylaniline (**1b**), diethyl malonate (**2**) and 4-methylbenzaldehyde (**5b**) were illustrated in Table 1. In **6b**; the two quinolinone rings are spectroscopically nonequivalent, although some of their signals co-resonate; the simplest explanation is that their rotation is hindered so that the compound does not possess a σ plane. The 6H methyl singlet at δ 2.38 must be H-6a; its attached carbon appears at δ 20.64. H-6a gives HMBC correlation with carbon signals at δ 131.91 and 122.03; these are assigned as C-7 and C-5 in that order, because the downfield of the two gives HSQC correlation with a 2H doublet at δ 7.42 and the upfield signal correlates with the nonequivalent 1H singlets at δ 7.79 and 7.69. C-7 also gives HMBC correlation with a 2H doublet at δ 7.33, assigned as H-8; its attached carbon appears at δ 115.34 grounds as C-2,2′,4,4′.

The *p*-tolyl group is assigned similarly: the 3H methyl singlet at δ 2.26 must be H-3f and gives HSQC correlation

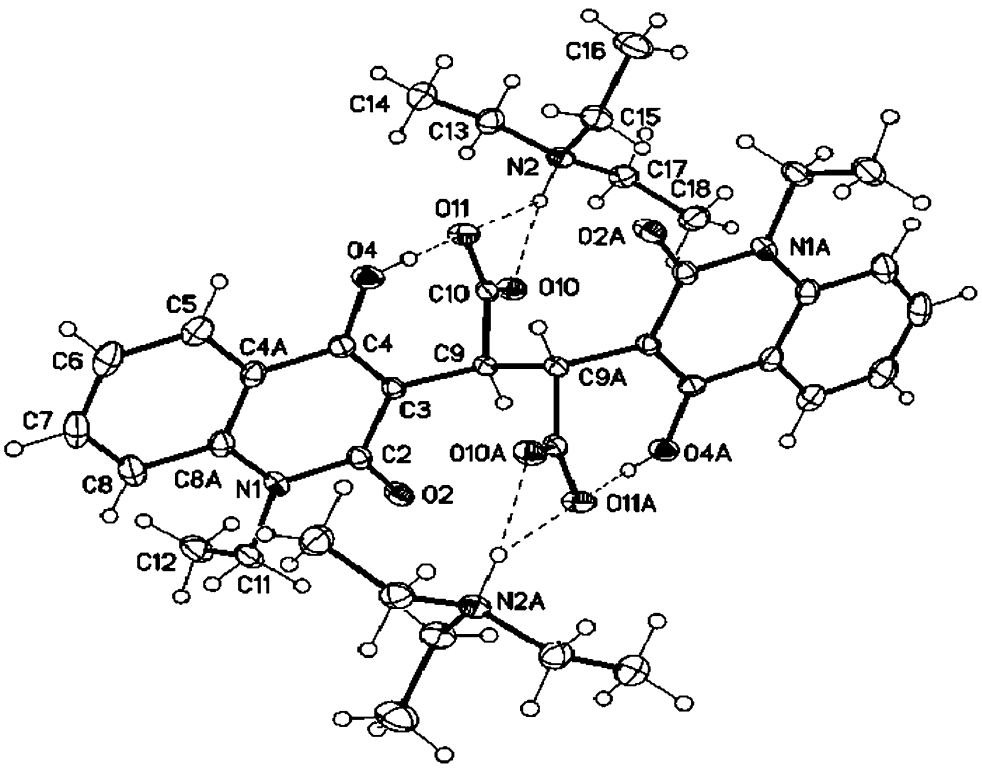
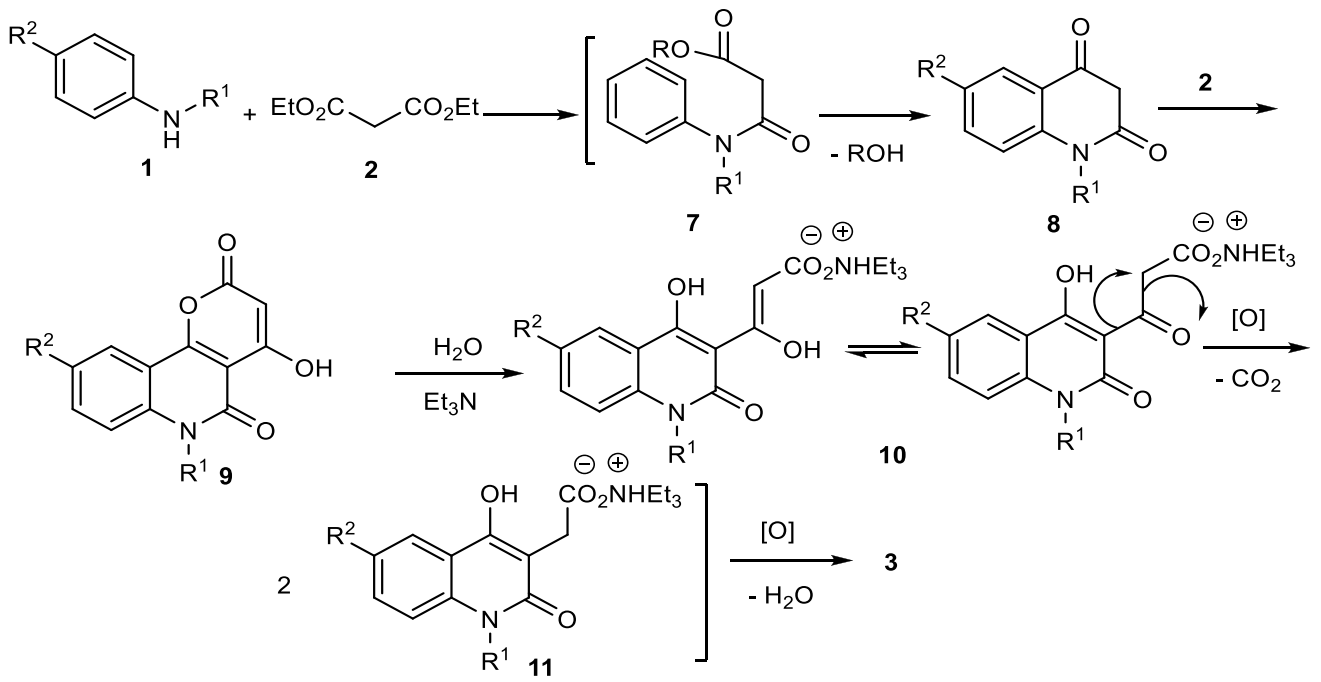


Fig. 2 Molecular structure analysis of compound **3d** (displacement parameters are drawn at 50% probability level)



Scheme 2 Proposed mechanism describes the formation of **3**

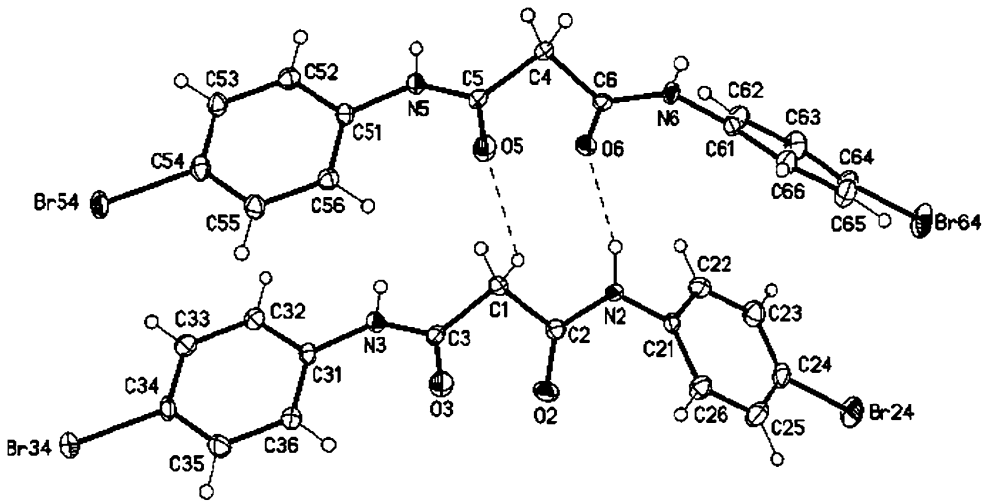


Fig. 3 Molecular structure analysis of compound **4** (displacement parameters are drawn at 50% probability level)

to a carbon at δ 20.02. C-3f gives HMBC correlation to a 2H doublet at δ 7.05, assigned as H-3d; its attached carbon appears at δ 128.14. H-3d gives COSY correlation with the remaining 2H doublet at δ 6.96; its attached carbon appears at δ 125.66. H-3c, H-3d, and C-3c also give HMBC correlation with the 1H singlet at δ 6.10, assigned as H-3a; its attached carbon appears at δ 34.43. The four lines between δ 166–160 give HMBC correlation with H-3a and are assigned on chemical-shift. The remaining ^{13}C lines are assigned on chemical shifts as shown in the Table 1. Finally, an X-ray structure analysis of compound **6**e was obtained after recrystallization from *N*,*N*-dimethylformamide and ethanol; the structure showed the inclusion of a molecule of DMF (Fig. 5).

The mechanism can be explained as due to formation of 2-quinolone **8** by the same previous steps mentioned in Scheme 2. Compound **8** would then condense with aldehyde **5** to give intermediate **12** (Scheme 3). Elimination of water molecule from **12** would enable the formation of **13**. Addition of another one molecule of **8**–**13** would ultimately give **6** (Scheme 3).

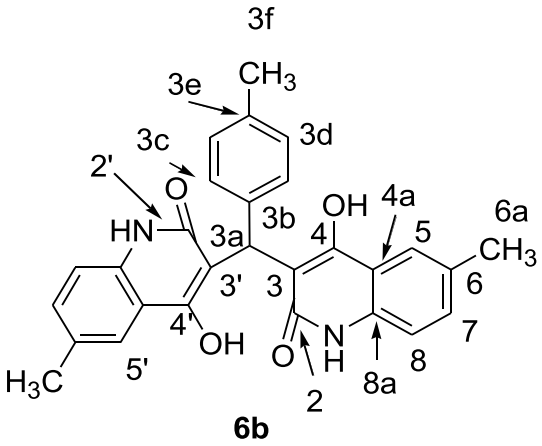


Fig. 4 Magnetically inequivalent carbons of compound **6b**

Experimental

Melting points were determined using open glass capillaries on a Gallenkamp melting point apparatus (Weiss–Gallenkamp, Loughborough, UK) and are uncorrected. The IR spectra were recorded from potassium bromide disks with a FT device, Minia University. NMR spectra were measured in DMSO-d_6 on a Bruker AV-400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C, and 40.55 MHz for ^{15}N); chemical shifts are expressed in δ (ppm), versus internal tetramethylsilane (TMS) = 0 for ^{1}H and ^{13}C, and external liquid ammonia = 0 for ^{15}N. Coupling constants are stated in Hz. Correlations were established using ^{1}H-^{1}H COSY, and ^{1}H-^{13}C and ^{1}H-^{15}N HSQC and HMBC experiments. Mass spectra were recorded on a Finnigan Fab 70 eV, Institute of Organic Chemistry, Karlsruhe University, Karlsruhe, Germany. TLC was performed on analytical Merck 9385 silica aluminum sheets (Kieselgel 60) with Pf_{254} indicator; TLCs were viewed at λ_{max} = 254 nm. Elemental analyses were carried out at the Microanalytical Center, Cairo University, Egypt.

General procedure describes the formation of compounds 3a–d

A mixture of aromatic amines **1a–d** (1 mmol) and **2** (2 mmol) in 50 mL of diphenyl ether and 0.5 mL of Et_3N was heated at 180 °C for 4 h. The formed resulting white precipitate was left to cool for 24 h. The precipitate was

Table 1 NMR spectral data of compound **6b**

^{1}H NMR	^{1}H-^{1}HCOSY	Assignment
13.18 (s; 1H), 12.73 (s; 1H)		OH
12.21 (s; 1H), 12.10 (s; 1H)		NH
7.79 (s; 1H), 7.69 (s; 1H)	7.42,7.33,*2.38*	H-5,5′
7.42 (d, *J* = 8.0; 2H)	7.79,7.69,7.33,*2.38*	H-7
7.33 (d, *J* = 8.4; 2H)	7.79, 7.69, 7.42	H-8
7.05 (d, *J* = 7.2; 2H)	6.96, 6.10, 2.26	H-3d
6.96 (d, *J* = 7.6; 2H)	7.05, 6.10	H-3c
6.10 (s; 1H)	7.05, 6.96, 2.26	H-3a
2.38 (s; 6H)	7.79, 7.69, 7.42	H-6a
2.26 (s; 3H)	7.05, 6.10	H-3f

^{13}C NMR	HSQC	HMBC	Assignment
165.87, 164.17		6.10	C-2,2′
161.64, 160.69	6.10		C-4,4′
134.56, 134.14, 134.05	7.42,7.05, 6.96, 6.10, 2.26		C-3b,4a,6
131.91	7.42	7.33, 2.38	C-7
131.24			C-8a
128.14	7.05	7.05, 2.26	C-3d
125.66	6.96	6.96, 6.10	C-3c
122.03	7.79, 7.69	7.42, 2.38	C-5
115.99			C-3e
115.34	7.33	7.33	C-8
110.85, 109.22	6.96		C-3,3′
34.43	6.10	6.96	C-3a
20.64	2.38	7.42	C-6a
20.02	2.26	7.05	C-3f

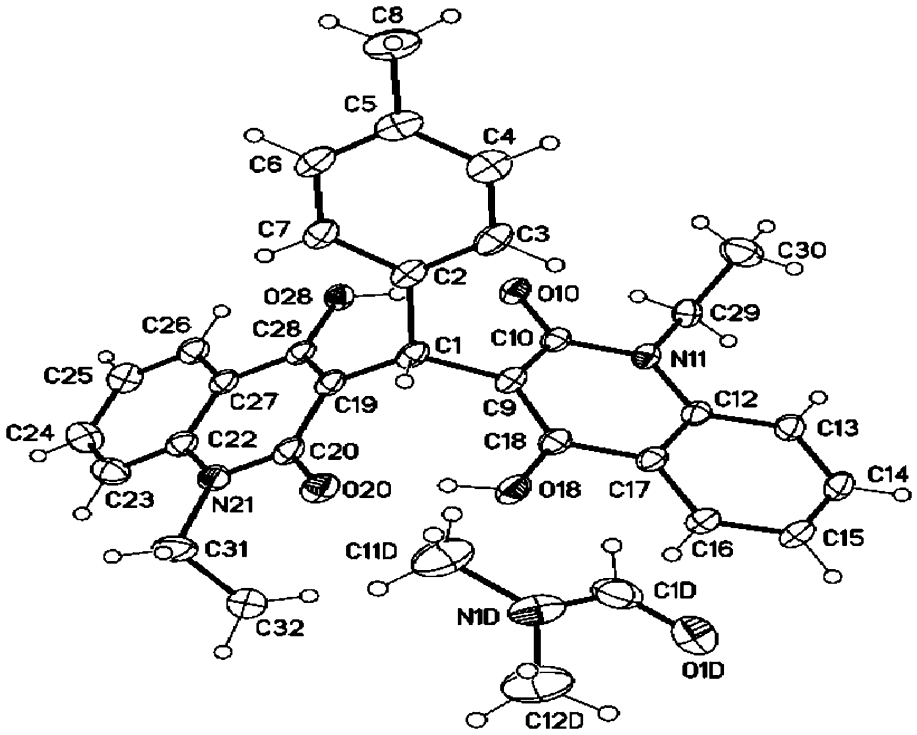
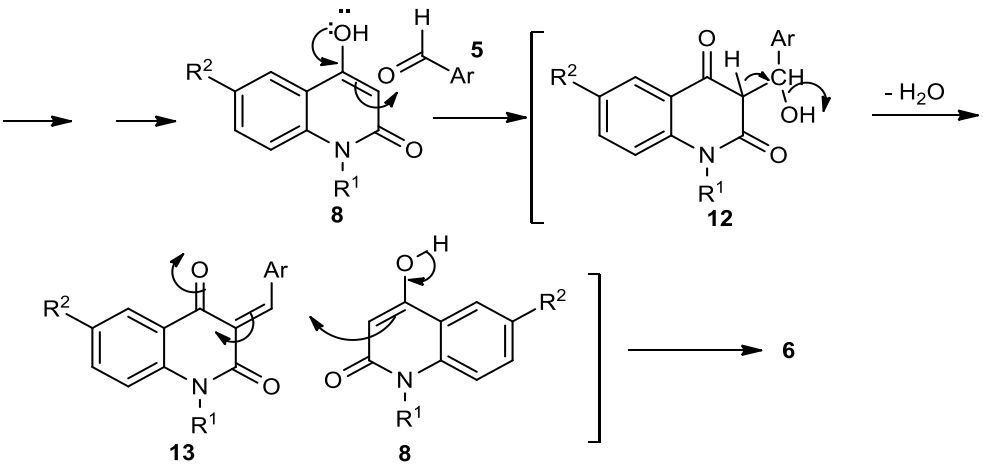


Fig. 5 Molecular structure of compound **6e** (displacement parameters are drawn at 50% probability level)



Scheme 3 Suggested mechanism describes the formation of **6**

collected by filtration, then was washed with 200 mL of EtOH and then dried well. The formed product was then recrystallized from stated solvents.

(2*R*,3*S*)-2,3-bis(4-hydroxy-2-oxo-1,2-dihydro-quinolin-3-yl)succinate. bis(triethylammonium) salt (3a)

Yellow crystals (DMF), 0.35 g (80%), m.p. 340–2 °C (decomp).

IR (KBr): $\bar{\upsilon} = 3400$ (OH), 3210 (NH), 3030–3000 (Ar–CH), 2980–2670 (Aliph–CH), 1720, 1680 cm^{-1} (CO); ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 14.10$ (s, 2H, 2COOH), 13.20 (s, 2H, 2OH), 11.80 (s, 2H, 2NH), 8.08 (dd, 2H, $J = 1.0$, 0.8 Hz), 7.60–7.56 (m, 2H), 7.40–7.33 (m, 4H), 3.72 (s, 2H), 3.17 (q, 12H, $6CH_2$–NEt_3), 1.30 ppm (t, 18H, $6CH_3$–$2NEt_3$); ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 164.8$ (2CO-acid), 160.1 (2CO-quinolone), 158.0 (Ar–2C–OH), 146.7 (Ar–2C), 133.6, 122.9, 122.8, 116.8 (Ar–2H), 111.7,

105.4 (Ar–2C), 50.0 ($6CH_2$–NEt_3), 38.2 (Aliph–2CH), 13.7 ppm ($6CH_3$–NEt_3).

MS (70 eV, %): *m/z* = 436 (M–$2Et_3N$, 100), 306 (30), 282 (52), 153 (92), 136 (65), 106 (25).

Anal for $C_{34}H_{46}N_4O_8$ (638.75): Calcd. 63.93; H, 7.26; N, 8.77. Found: C, 64.00; H, 7.30; N, 8.80.

(2*R*,3*S*)-2,3-bis(4-hydroxy-6-methyl-2-oxo-1,2-dihydroquinolin-3-yl)-succinate. bis(triethyl-ammonium) salt (3b)

Yellow crystals (DMF/EtOH), 0.39 g (84%), m.p. 350–2 °C.

IR (KBr): $\bar{\upsilon}$ = 3460 (OH), 3230 (NH), 3060–3030 (Ar–CH), 2970–2890 (Aliph–CH), 1718, 1682 cm^{-1} (CO). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 14.20 (s, 2COOH), 13.20 (s, 2H, 2OH), 11.20 (s, 2H, 2NH), 8.15 (d, 2H, *J* = 0.7 Hz), 7.77–7.74 (m, 2H), 6.80 (dd, 2H, *J* = 1.1 Hz), 3.75 (bs, 2H), 3.20 (q, 12H, $6CH_2$), 2.20 (s, 6H, $2CH_3$), 1.20 ppm (t, 18H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.6 (2CO–ester), 162.3 (2CO–quinolone), 158.4 (Ar–2C–OH), 147.2, 137.2, 133.3 (Ar–2C), 126.8, 123.4 (Ar–2H), 112.4, 106.0 (Ar–2C), 50.0 ($6CH_2$–Et_3N), 37.4 (Aliph–2CH), 21.0 ($2CH_3$) 14.4 ppm ($2CH_3$–ester).

MS (70 eV, %): *m/z* = 465 (M–$2Et_3N^+$, 100), 442 (18).

Anal for $C_{36}H_{50}N_4O_8$ (660.80): Calcd. 64.84; H, 7.56; N, 8.40. Found: C, 64.80; H, 7.60; N, 8.76.

(2*R*,3*S*)-2,3-bis(6-chloro-4-hydroxy-2-oxo-1,2-dihydro-quinolin-3-yl)succinate. Bis(triethyl-ammonium) salt (3c)

Yellow crystals (DMF/EtOH), 0.40 g (79%), m.p. 310–2 °C.

IR (KBr): $\bar{\upsilon}$ = 3400 (OH), 3220 (NH), 3060–3030 (Ar–CH), 2970–2890 (Aliph–CH), 1715, 1672 cm^{-1} (CO). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 14.20 (s, 2H, 2COOH), 13.20 (s, 2H, 2OH), 11.80 (s, 2H, 2NH), 7.80 (d, 2H, *J* = 0.7 Hz), 7.40 (dd, 2H, *J* = 1.2, 0.8 Hz), 7.15 (dd, 2H, *J* = 1.1, 0.7 Hz, Ar–H), 3.80 (s, 2H), 3.20 (q, 12H, CH_2–Et_3N), 1.20 ppm (t, 18H, CH_3–NEt_3).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 168.2 (2CO–acid), 162.0 (2CO–quinolone), 157.6 (Ar–2C–OH), 141.6, 135.6, 133.2 (Ar–2C), 128.6, 127.4 (Ar–2H), 113.4, 101.4 (Ar–2C), 50.0 ($6CH_2$–NEt_3), 38.0 (Aliph–2CH), 13.0 ppm ($6CH_3$–ester).

MS (70 eV, %): *m/z* = 505 (M^+, 15), 153 (37), 135 (25), 101 (100).

Anal for $C_{34}H_{44}Cl_2N_4O_8$ (707.64): Calcd. 57.71; H, 6.27; N, 7.92. Found: C, 57.80; H, 6.30; N, 8.00.

(2*R*,3*S*)-2,3-bis(1-ethyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)succinate. bis(triethylammonium) salt (3d)

Yellow crystals (AcOEt), 0.41 g (82%), m.p. > 350 °C.

IR (KBr): $\bar{\upsilon}$ = 3450–3360 (OH), 3220 (NH), 3060–3020 (Ar–CH), 2960–2810 (Aliph–CH), 1716, 1665 cm^{-1} (CO).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 14.20 (s, 2H, COOH), 13.30 (s, 2H, 2OH), 7.40–7.35 (m, 4H), 7.25–7.22 (m, 4H), 3.70 (s, 2H), 3.20 (q, 12H, $6CH_2$–NEt_3), 3.15 (q, 4H, $2CH_2$–NEt_3), 1.17 (t, 6H, $2CH_3$–Et_3N), 1.15 ppm (t, 18H, $6CH_3$–Et_3N).

^{13}C NMR (100 MHz, DMSO-d_6): couldn't be resolved due to bad solubility.

MS (70 eV, %): *m/z* = 492 (M^+, 35), 472 (40), 306 (42), 153 (100), 136 (72).

Anal for $C_{38}H_{54}N_4O_8$ (694.86): Calcd. 65.68; H, 7.83; N, 8.06. Found: C, 65.80; H, 7.70; N, 8.15.

Preparation of compound 4

On repeating the previous procedure, a mixture of aromatic amine **1e** (340 mg, 2 mmol) and **2b** (160 mg, 1 mmol) in 15 mL of diphenyl ether and 0.5 mL of Et_3N was heated at 180 °C for 4 h. The resulting pale-yellow precipitate was left to cool. The formed product was then recrystallized.

N^1,N^3-bis(4-bromophenyl)malonamide (**4**). Pale yellow crystals (MeOH), 0.40 g (95%), m.p. 330–2 °C (lit (Vennerstrom and Holmes 1987), 332 °C).

IR (KBr): $\bar{\upsilon}$ = 3230 (NH), 3090–3030 (Ar–CH), 2970–2820 (Aliph–CH), 1685 cm^{-1} (CO).

MS (70 eV, %): *m/z* = 414 (M^{+2}, 18), 412 (M^+, 30), 239 (40), 172 (100).

General procedure describes the formation of compounds 6a–e

On repeating the procedure, a mixture of aromatic amines **1a–d** (2 mmol), **2b** (320 mg, 2 mmol) and aromatic aldehydes **5a–c** (1 mmol) in 70 mL of diphenyl ether and 0.5 mL of Et_3N was fused at 180 °C for 4 h. The resulting white precipitate was left to cool and then poured in ice-cold saturated solution of $NaHCO_3$. The formed precipitate was kept standing up at room temperature for 24 h. The precipitate which was collected by filtration was washed with about 200 mL of H_2O. The formed product was then washed again with 200 mL of EtOH and dried well. The formed product was then recrystallized from stated solvents.

3,3′-(Phenylmethylene)bis(4-hydroxyquinolin-2(1*H*)-one (6a)

Yellow crystals (DMF/EtOH), 0.360 g (88%), m.p. 335–7 °C.

IR (KBr): $\tilde{\upsilon}$ = 3390 (OH), 3230 (NH), 3070 (Ar–CH), 2970 (Aliph–CH), 1650 (CO), 1605, 1580 cm^{-1} (C=C); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 13.17 (s; 1H, OH), 12.70 (s, 1H, OH), 12.22 (s, 1H, NH), 12.11 (s, 1H, NH), 7.80 (d 2H, H-5,5′), 7.67 (m 2H, H-6,6′), 7.44 (m 2H, H-7,7′), 7.30 (d 2H, H-8,8′), 7.05–6.96 (m 5H, Ph-H), 6.11 ppm (s; 1H, H-3a).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.71, 164.11 (C-2,2′), 161.33, 160.77 (C-4,4′), 135.60 (C-3b), 134.11 (C-4a), 131.22 (C-7), 130.89 (C-8a), 122.89, 122.86, 116.78 (Ph-CH), 115.11 (C-3,3′), 34.32 ppm (C-3a).

MS (70 eV, %): *m/z* = 410 (M^+, 34), 333 (100), 161 (55), 77 (66).

Anal for $C_{25}H_{18}N_2O_4$ (410.42): Calcd. C, 73.16; H, 4.42; N, 6.83. Found: C, 73.22; H, 4.36; N, 6.95.

3,3′-(4′-Methylphenyl-methylene) bis(4-hydroxy-6-methyl-quinolin-2(1*H*)-one (6b)

Yellow crystals (DMF/EtOH), 0.365 g (80%), m.p. 358–60 °C.

IR (KBr): $\tilde{\upsilon}$ = 3410 (OH), 3222 (NH), 3045–3020 (Ar–CH), 2989 (Aliph-CH), 1646 (CO), 1610, 1590 cm^{-1} (C=C).

NMR (400 MHz, DMSO-d_6) (Table 1).

MS (70 eV, %): *m/z* = 452 (M^+, 38), 361 (100), 187 (24), 91 (66).

Anal for $C_{28}H_{24}N_2O_4$ (452.50): Calcd. C, 74.32; H, 5.35; N, 6.19. Found: C, 74.22; H, 5.43; N, 6.35.

3,3′-(4′-Methylphenyl-methylene)bis(4-hydroxy-quinolin-2(1*H*)-one (6c)

Yellow crystals (DMF/EtOH), 0.360 g (88%), m.p. > 360 °C.

IR (KBr): $\tilde{\upsilon}$ = 3405 (OH), 3225 (NH), 3091 (Ar–CH), 2956 (Aliph–CH), 1648 (CO), 1600, 1590 cm^{-1} (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 13.11 (s 1H, OH), 12.78 (s 1H, OH), 12.20 (s 1H, NH), 11.99 (s 1H, NH), 7.81, 7.76 (m, 2H, H-5,5′), 7.42 (m 2H, H-7), 7.03 (d *J* = 7.1 Hz, 2H, H-3d), 6.98 (m 2H, H-3c), 6.12 (s, 1H, H-3a), 2.23 ppm (s, 3H, H-3f).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.80, 164.21 (C-2,2′), 161.63, 159.97 (C-4,4′), 135.55 (C-3b), 134.18 (C-4a), 132.01 (C-8a), 128.66 (C-6), 128.21 (C-3d), 125.08 (C-3c), 123.11 (C-5), 115.78 (C-3e), 115.55 (C-8), 110.99 (C-3,3′), 34.33 (C-3a), 20.10 ppm (C-3f).

MS (70 eV, %): *m/z* = 424 (M^+, 40), 333 (100), 161 (67), 77 (77).

Anal for $C_{26}H_{20}N_2O_4$ (424.45): Calcd. C, 73.57; H, 4.75; N, 6.60. Found: C, 73.65; H, 4.71; N, 6.51.

3,3′-((4-chlorophenyl)methylene) bis(4-hydroxy-6-methylquinolin-2(1*H*)-one) (6d)

Yellow crystals (DMF/EtOH), 0.32 g (68%), m.p. 280–2 °C.

IR (KBr): $\tilde{\upsilon}$ = 3385 (OH), 3210 (NH), 3077 (Ar–CH), 2980 (Aliph-CH), 1646 (CO), 1605, 1588 cm^{-1} (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 13.21 (s, 1H, OH), 12.70 (s; 1H, OH), 12.21 (s, 1H, NH), 12.08 (s, 1H, NH), 7.77 (s, 2H, H-5,5′), 7.40 (d, *J* = 7.80 Hz, 2H, H-7), 7.03 (d, *J* = 7.0 Hz, 2H, H-3d), 6.97 (d, *J* = 7.2 Hz, 2H, H-3c), 6.10 (s, 1H, H-3a), 2.33 ppm (s, 6H, H-6a).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.67, 164.20 (C-2,2′), 161.66, 160.13 (C-4,4′), 135.54 (C-3b), 134.18 (C-4a), 134.09 (C-6), 131.87 (C-7), 131.11 (C-8a), 130.32 (C-3e), 128.22 (C-3d), 125.18 (C-3c), 122.32 (C-5), 115.48 (C-8), 110.90, 109.66 (C-3,3′), 34.30 (C-3a), 20.55 ppm (C-6a).

MS (70 eV, %): *m/z* = 472 (M^+, 71), 361 (100), 187 (67), 111 (43), 77 (65).

Anal for $C_{27}H_{21}ClN_2O_4$ (472.92): Calcd. C, 68.57; H, 4.48; Cl, 7.50; N, 5.92. Found: C, 68.65; H, 4.55; N, 6.11.

3,3′-(*p*-Tolylmethylene)bis(1-ethyl-4-hydroxy-quinolin-2(1*H*)-one (6e)

Yellow crystals (DMF/EtOH), 0.400 g (83%), m.p. 312–4 °C.

IR (KBr): $\tilde{\upsilon}$ = 3390 (OH), 3220 (NH), 3052 (Ar–CH), 2988 (Aliph–CH), 1649 (CO), 1600, 1580 cm^{-1} (Ar–C=C).

MS (70 eV, %): *m/z* = 480 (M^+, 71), 389 (100), 189 (32), 91 (43), 77 (50).

Anal for $C_{30}H_{28}N_2O_4$ (480.55): Calcd. C, 74.98; H, 5.87; N, 5.83. Found: C, 75.15; H, 5.75; N, 6.01.

Supporting information

Crystal structure determinations

The single-crystal X-ray diffraction studies were carried out on a Bruker D8 Venture diffractometer with Photon100 detector at 123(2) K using Cu-Kα radiation (**3d**, **6e**, λ = 1.54178 Å) or Mo-Kα radiation (**4**, λ = 0.71073 Å). Direct Methods (**3d**, **6e**, SHELXS-97) (Sheldrick 2008) or dual space methods (**4**, SHELXT for **5a**) (Sheldrick 2015) were used for structure solution and refinement was carried out using SHELXL-2014 (full-matrix least-squares on F^2) (Sheldrick 2015). Hydrogen atoms were localized by difference electron density determination and refined using a riding model (H(O, N) free). Semi-empirical absorption corrections were applied. For **4** and **6e** an extinction of

corrections was applied. In **6e** one NEt-group is disordered. The absolute structure of **4** was determined by refinement of Parsons' *x*-parameter (Parson et al. 2013).

3d: colorless crystals, $C_{26}H_{22}N_2O_8^{2-} \bullet 2(C_6H_{16}N)^+$, $M_r = 694.85$, crystal size $0.18 \times 0.14 \times 0.12$ mm, monoclinic, space group $P2_1/c$ (No. 14), $a = 9.9912(3)$ Å, $b = 10.7399(3)$ Å, $c = 16.4621(4)$ Å, $\beta = 94.647(1)°$, $V = 1760.65(8)$ Å^3, $Z = 2$, $\rho = 1.311$ Mg/m^{-3}, μ(Cu-K$_\alpha$) = 0.747 mm^{-1}, $F(000) = 748$, $2\theta_{max} = 144.2°$, 17106 reflections, of which 3467 were independent ($R_{int} = 0.025$), 232 parameters, 2 restraints, $R_1 = 0.039$ (for 3201 $I > 2\sigma(I)$), w$R_2 = 0.106$ (all data), $S = 1.03$, largest diff. peak/hole = 0.303/−0.237 e Å^{-3}.

4: colorless crystals, $C_{15}H_{12}Br_2N_2O_2$, $M_r = 412.02$, crystal size $0.28 \times 0.14 \times 0.05$ mm, orthorhombic, space group $Pca2_1$ (No. 29), $a = 9.5819(4)$ Å, $b = 18.4026(7)$ Å, $c = 16.9824(7)$ Å, $V = 2994.5(2)$ Å^3, $Z = 8$, $\rho = 1.828$ Mg/m^{-3}, μ(Mo-K$_\alpha$) = 5.419 mm^{-1}, $F(000) = 1616$, $2\theta_{max} = 55.4°$, 104279 reflections, of which 6908 were independent ($R_{int} = 0.048$), 392 parameters, 5 restraints, $R_1 = 0.028$ (for 6424 $I > 2\sigma(I)$), w$R_2 = 0.063$ (all data), $S = 1.08$, largest diff. peak/hole = 0.754/−0.420 e Å^{-3}, $x = 0.000(6)$.

6e: colorless crystals, $C_{30}H_{28}N_2O_4 \bullet C_3H_7NO$, $M_r = 553.64$, crystal size $0.38 \times 0.30 \times 0.24$ mm, monoclinic, space group $P2_1/c$ (No. 14), $a = 11.4000(5)$ Å, $b = 11.1444(5)$ Å, $c = 22.8990(9)$ Å, $\beta = 103.551(2)°$, $V = 2828.2(2)$ Å^3, $Z = 4$, $\rho = 1.300$ Mg/m^{-3}, μ(Cu-K$_\alpha$) = 0.711 mm^{-1}, $F(000) = 1176$, $2\theta_{max} = 144.0°$, 25228 reflections, of which 5552 were independent ($R_{int} = 0.023$), 379 parameters, 8 restraints, $R_1 = 0.037$ (for 5095 $I > 2\sigma(I)$), w$R_2 = 0.101$ (all data), $S = 1.05$, largest diff. peak/hole = 0.270/−0.245 e Å^{-3}.

CCDC 1824942 (**3d**), 1827436 (**4**), and 1824943 (**6e**) 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.

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