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The first entry to pyrrolo[2,3-*c*]quinoline-2,4(3a*H*,5*H*)-diones

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Dedicated to Professor Miha Tišler

Abstract

Wittig olefination of 3-aminoquinoline-2,4(1*H*,3*H*)-diones **1** with ethyl (triphenylphosphoranylidene)acetate ($Ph_3P{=}CHCO_2Et$) afforded (*E*)-3-amino-4-ethoxycarbonylmethylene-1,2,3,4-tetrahydro-2-quinolones (*E*)-**2** and pyrrolo[2,3-*c*]quinoline-2,4(3a*H*,5*H*)-diones **3**. An alternative approach for the synthesis of **3** via 3-bromoacetamidoquinoline-2,4(1*H*,3*H*)-diones **7**, their corresponding triphenylphosphonium salts **8**, and ylides **A** that undergo intramolecular Wittig reaction, was investigated. Under the applied reaction conditions, the phosphonium salts **8** and ylides **A** are so unstable that they partly decompose to 3-acetamidoquinoline-2,4(1*H*,3*H*)-diones **9** during the synthesis of **3**.

Keywords: Pyrrolo[2,3-*c*]quinolones; Quinolinones; Wittig olefination; Mechanism; NMR

1. Introduction

As a part of our continued interest in the reactivity of quinoline-2(1*H*)-ones,[1–5] we have reported their transformations to several *c*-fused derivatives of [1,3]thiazolo[5,4-*c*]quinolin-4(5*H*)-one,[1e] imidazo[4,5-*c*]quinolin-4(5*H*)-one,[3] furo[3,4-*c*]quinoline-3,4(1*H*,5*H*)-dione,[1h] and furo[2,3-*c*]quinolin-4(5*H*)-one[1g,4] ring systems. The furo[2,3-*c*]quinolin-4(5*H*)-one skeleton, for example, has been the result of C-4 Wittig olefination of 3-hydroxyquinoline-2,4(1*H*,3*H*)-dione with ethyl (triphenylphosphoranylidene)acetate ($Ph_3P{=}CHCO_2Et$) and subsequent lactonization. An alternative approach via intramolecular Wittig reaction has also been shown.[5] The smooth reactivity of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones stimulated our interest in further studies on the closely related 3-aminoquinoline-2,4(1*H*,3*H*)-diones, for which we expected that the C-4 Wittig olefination with $Ph_3P{=}CHCO_2Et$ and subsequent lactamization might afford the corresponding pyrrolo[2,3-*c*]quinoline-2,4(3a*H*,5*H*)-diones.

In general, very few synthetic procedures leading to pyrrolo[2,3-*c*]quinolones have been reported,[6] despite the fact that this ring system occurs in certain pharmacologically active compounds.[7] To the best of our knowledge, however, there are no reports in the literature for pyrrolo[2,3-*c*]quinoline-2,4(3a*H*,5*H*)-diones.

2. Results and discussion

Starting 3-butylamino and 3-aminoquinoline-2,4(1*H*,3*H*)-diones **1** used in this work were prepared by literature procedures.[2] Wittig reactions of **1** with $Ph_3P{=}CHCO_2Et$ were conducted in boiling xylene (≈140 °C). In most cases, two types of products were formed and were isolated from the reaction mixtures, the desired pyrrolo[2,3-*c*]quinoline-2,4(3a*H*,5*H*)-diones **3** and (*E*)-4-ethoxycarbonylmethylene-3-amino-1,2,3,4-tetrahydroquinoline-2-ones, (*E*)-**2** (Scheme 1, Table 1). Considerable quantities of starting material **1** remained unconsumed and were recovered. Unfortunately,

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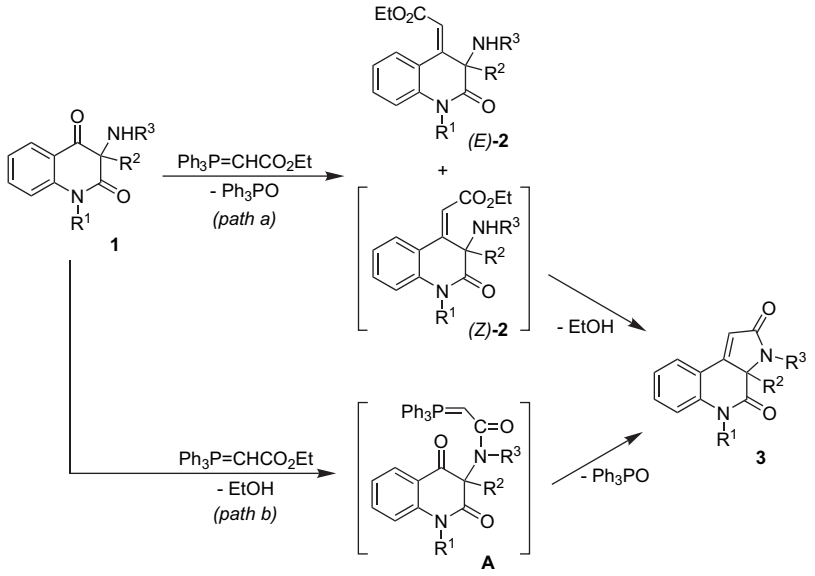


Scheme 1.

attempts to force the transformation forward and to increase the yields of **3** were rather unsuccessful. Prolonged reaction times resulted mostly in complex mixtures of products (entries 8 and 9, Table 1), and elevating the reaction temperature by changing the solvent from xylene to boiling decane (≈174 °C) or cymene (≈177 °C) had no desired effect (compare entries 2–4, Table 1).

It could be expected that the Wittig olefination of **1** initially affords both (*E*)-**2** and (*Z*)-**2**, and that the latter, under the applied reaction conditions spontaneously lactamizes to **3** (Scheme 1, *path a*). Alternatively, an intramolecular Wittig reaction of the intermediately formed ylide **A** (*path b*) via transamination cannot be ruled out.

As seen from Table 1, the choice of R^3 substituent in compounds **1** mostly affected the outcome of the reaction with $Ph_3P{=}CHCO_2Et$. In general, the yields of both **2** and **3** decreased when R^3 was changed from H to the bulkier *n*-butyl group.

The transformations of **1** to **3** were accompanied by the formation of byproducts, and in a few cases we were successful in isolating and identifying these byproducts (Chart 1, Table 1, entries 7–9).

Moderate yields of the desired pyrrolo[2,3-*c*]quinoline-2,4(3a*H*,5*H*)-diones **3** obtained from **1** and $Ph_3P{=}CHCO_2Et$ prompted us to search for an alternative approach, via an intramolecular Wittig reaction shown in Scheme 2.

The bromoacetamide derivatives **7** were obtained in relatively good yields from amines **1** and bromoacetyl bromide in benzene by using potassium carbonate as a base (Table 2). An exception was **1e**, which under the above reaction conditions did not react at all. Changing the reaction conditions to tetrahydrofuran as solvent and triethylamine as base at room temperature, the bromoacetylation of **1e** was extremely slow (2 days) and was accompanied by the consumption of large quantities of bromoacetyl bromide and triethylamine (see Section 3). Along with bromoacetamide **7e** (43% yield, Table 2,

Table 1
Reaction of **1a–k** with $Ph_3P{=}CHCO_2Et$

Entry	1	Substituents			Solvent	Time (h)	Product, yield[a] (%)			
		R^1	R^2	R^3			1[b]	2	3	Other
1	**a**	H	*n*-C_4H_9	H	Xylene	5	14	37	23	
2	**b**	H	*n*-C_4H_9	*n*-C_4H_9	Xylene	7	89	7	3	
3					Decane	6	67	24	—	
4					Cymene	7	47	14	—	
5	**c**	H	CH_2Ph	H	Xylene	4	20	35	32	
6	**d**	H	CH_2Ph	*n*-C_4H_9	Xylene	4	9	—	4	
7	**e**	H	Ph	H	Xylene	6	11	42	9	**5e** (6)
8					Xylene	36	—	31	—	**5e** (8)
9	**f**	H	Ph	*n*-C_4H_9	Xylene	58	—	—	—	**4f** (9), **5f** (8), **6f** (22)
10	**g**	CH_3	Ph	H	Xylene	4	29	27	10	
11	**h**	CH_3	Ph	*n*-C_4H_9	Xylene	4	21	54	10	
12	**i**	Ph	CH_3	H	Xylene	6	—	29	9	
13	**j**	Ph	CH_3	*n*-C_4H_9	Xylene	10	2	2	10	
14	**k**	CH_2Ph	Ph	*n*-C_4H_9	Decane	21	—	14[c]	—	

[a] Yield of isolated and re-crystallized products is given.
[b] Recovered starting material.
[c] Isolated as the hydrochloride salt.

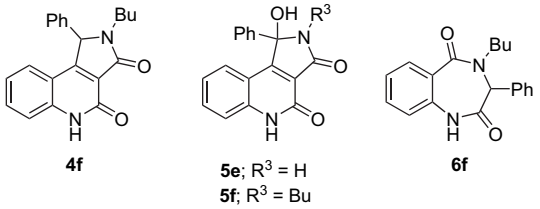
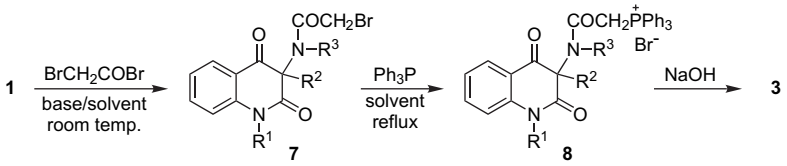


Chart 1.



Scheme 2.

entry 5), we isolated from the reaction mixture large amounts of 4-bromobutyl bromoacetate, which was a result of reaction between tetrahydrofuran and bromoacetyl bromide.[8,9] The low reactivity of amine **1e** in tetrahydrofuran is remarkable as other amines tested (**1f** and **1i**) transformed to the corresponding bromoacetamides (**7f** and **7i**) much faster, and consequently, lower excesses of bromoacetyl bromide were required. For the preparation of **7e** from **1e**, a dichloromethane/triethylamine system (Table 2, entry 8) finally gave acceptable results in terms of both reaction time and yield.

Table 2
Synthesis of bromoacetamides **7a**–**j** from **1**

Entry	Product 7	Substituents			Base/solvent	Time (h)	Yield[a] (%)
		R^1	R^2	R^3			
1	**a**	H	*n*-C_4H_9	H	K_2CO_3/benzene	2	74
2	**b**	H	*n*-C_4H_9	*n*-C_4H_9	K_2CO_3/benzene	2	72
3	**c**	H	CH_2Ph	H	K_2CO_3/benzene	2	86
4	**d**	H	CH_2Ph	*n*-C_4H_9	K_2CO_3/benzene	2	74
5	**e**	H	Ph	H	Et_3N/THF	[b]	43
6					Et_3N/CH_2Cl_2	[b]	69
7	**f**	H	Ph	*n*-C_4H_9	K_2CO_3/benzene	2	22
8					Et_3N/THF	[b]	27
9	**g**	CH_3	Ph	H	K_2CO_3/benzene	2	53
10	**h**	CH_3	Ph	*n*-C_4H_9	K_2CO_3/benzene	2	92
11	**i**	Ph	CH_3	H	Et_3N/THF	[b]	44
12	**j**	Ph	CH_3	*n*-C_4H_9	K_2CO_3/benzene	2	36

[a] Yield of isolated and re-crystallized products is given.
[b] For details, see Section 3.

Table 3
Synthesis of phosphonium salts **8a**,**c**,**e**–**g**,**i** from **7**

Educt 7	Solvent	Time (h)	Product, yield[a] (%)	
			8	Other
a	Benzene	6	72	
c	Benzene	6	48	**9c** (9)
e	1,4-Dioxane	13	62	
f	Benzene	4.5	24	
g	Benzene	6	52	**9g** (22)
i	Benzene	8	26	**9i** (29), **3i** (3)

[a] Yield of isolated and re-crystallized products is given.

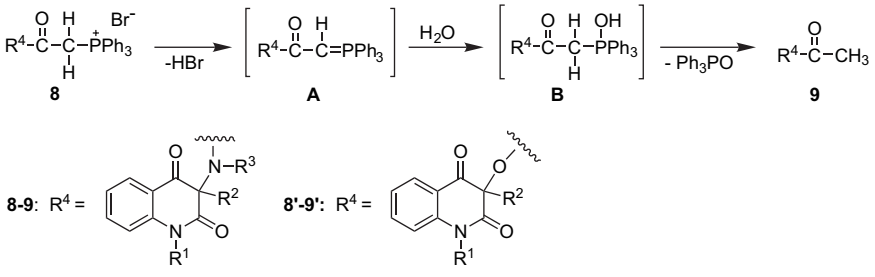
The phosphonium salts **8** were then prepared by heating bromoacetamides **7** and triphenylphosphine in boiling benzene (Scheme 2, Table 3). Along with compounds **8**, we isolated substantial amounts of acetamides **9**. The fact that during the isolation workup some phosphonium salts **8** spontaneously eliminated HBr, accompanied by the formation of **9**, indicated high acidity of the PCH_2 methylene protons and facile formation of ylide **A**. The addition of a water molecule (ambient moisture) to **A** likely gives intermediate **B** and finally acetamide **9**, as shown in Scheme 3.[10]

Interestingly, in those instances where R^3 was the *n*-butyl moiety, the phosphonium salts **8** also formed (vide infra), but were so reactive that we were unable to isolate them from the reaction mixtures. Any attempt to isolate **8b**,**d**,**h**,**j** resulted in complete conversion to acetamides **9b**,**d**,**h**,**j**. The exception was **8f**. Under the above reaction conditions, compound **7e** did not form phosphonium salt **8e**. Better results were obtained when the reaction was conducted in boiling 1,4-dioxane (See Table 3 and Section 3).

The above discussed reactivity of phosphonium salts **8** was unexpected as during the synthesis of analogous furo[2,3-*c*]-quinoline-2,4(3a*H*,5*H*)-diones via intramolecular Wittig reaction of **8′**, using the same reaction and workup procedures, the corresponding hydrolytic products **9′** were not observed at all.[5]

In the last step of the transformation, either the isolated phosphonium salts (**8a**,**c**,**e**,**f**,**g**,**i**) or the in situ formed compounds (**8b**,**d**,**h**,**j**) were transformed to the ylides in a two-phase chloroform/aq NaOH system. The ylides spontaneously transformed further to pyrrolo[2,3-*c*]quinoline-2,4(3a*H*,5*H*)-diones **3**. The reactions were generally accompanied by the formation of **9**, confirming the mechanism in Scheme 3 (Table 4).

Analyses of IR, ^1H, and ^{13}C NMR spectra and in some cases NOE, 2D NMR ($^1H-^1H$ COSY, $^1H-^{13}C$ HMQC, and HMBC), mass spectra, and CHN elemental analyses confirmed the structures of compounds under investigation.



Scheme 3.

Table 4
Synthesis of **3** by intramolecular Wittig reaction

Entry	Educt	Method[b]	Product, yield[a] (%)	
			3	**9**
1	**8a**	A	52	10
2	**7b**	B	25	68
3	**8c**	A	88	9
4	**7d**	B	39	25
5	**8e**	A	51	—
6	**8f**	A	28	—
7	**8g**	A	62	5
8	**7h**	B	12	69
9	**7j**	B	—	60

[a] Yield of isolated and re-crystallized products is given.
[b] Method A: **8**, aq NaOH/$CHCl_3$, 5 min. Method B: **7**, Ph_3P, benzene, reflux 4 h then NaOH/$CHCl_3$, 5 min (one pot).

Pyrrolo[2,3-*c*]quinoline-2,4(3a*H*,5*H*)-diones **3** show characteristic light blue fluorescence at λ 254 and λ 366 nm. In their IR spectra, characteristic absorption bands appear at 1660–1707 and 1597–1609 cm^{-1} (two lactam groups) and 1600–1608 cm^{-1} (C=C double bonds). Proton resonance for H-1 appearing at δ 5.91–6.63 ppm (d, J 0–1.2 Hz) and carbon resonance for C-3a at δ 64.8–73.9 are characteristic of compounds **3**. In the HMBC spectrum of pyrrolo[2,3-*c*]-quinoline-2,4(3a*H*,5*H*)-dione **3f**, proton H-1 shows correlations to carbon resonances at δ 73.9 (C-3a), 118.3 (C-9a), 155.4 (C-9b), 171.1 (C-2) ppm, as well as weak correlations to resonances at δ 137.2 (C-5a) and 135.6 (C-1″) ppm, as shown in Figure 1.

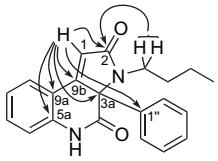
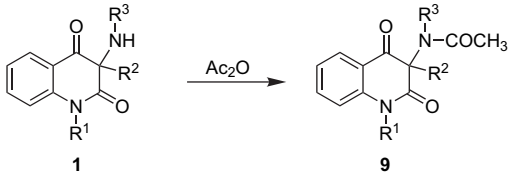


Figure 1. Selected HMBC correlations for **3f**.

The structures of acetamides **9** were confirmed by spectral analyses, as well as by independent preparation from **1** with acetic anhydride (Scheme 4, Table 5). The IR spectra of compounds **9** are very similar to those of bromoacetamido derivatives **7** and characteristic absorption bands of C=O groups appear at 1697–1712 cm^{-1} in both cases.



1 **9**

Scheme 4.

The suggested mechanism for the formation of isomeric pyrrolo[3,4-*c*]quinoline-3,4(2*H*,5*H*)-dione **4f**, shown in Scheme 5, comprises of an addition of carbanion to a transiently formed isocyanate group and subsequent enolization. An analogous isocyanate mechanism has been previously suggested for the rearrangement of furo[2,3-*c*]quinoline-2,4(3a*H*,5*H*)-diones to furo[3,4-*c*]quinoline-3,4(1*H*,5*H*)-diones.[1a,h] Another byproduct was isolated from the reaction of **1f** (Scheme 1, Table 1), and the structure of **5f** was assigned as the most plausible to it. Mechanistically, the formation of pyrrolo[3,4-*c*]quinoline-3,4(2*H*,5*H*)-diones **5** is conceivable by the aerial oxidation of **4**, as further depicted in Scheme 5. The easiness with which the oxidation of **4f** takes place is demonstrated by NMR experiment in which during ^{13}C NMR measurement, in 12 h period of time, approximately 50% of **4f** transformed into **5f**.

Table 5
Independent preparation of acetamides **9** from **1**

9	Solvent	Temperature	Time (h)	Yield[a] (%)
a	Py	rt	6	83
b	Py	rt	6	62
c	Py	rt	6	82
d	Py	60 °C	1	78
e	Toluene	Reflux then rt	4 and then 4	68
f	Toluene, Py	[b]	[b]	67
g	Py	60 °C	1	96
h	Py	60 °C	1	75
i	Py	60 °C	1	70
i	Toluene	[b]	[b]	70
j	Toluene	rt	[b]	62

[a] Yields of isolated and re-crystallized products are given.
[b] For details, see Section 3.

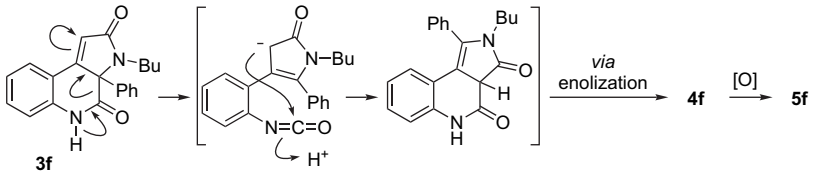
Ring expansion of a 3-aminoquinoline-2,4(1*H*,3*H*)-dione derivative to the corresponding diazepine has previously been documented by Podesva and co-workers[11] and explained by C-3/C-4 bond cleavage and subsequent lactamization mechanism. An alternative to the latter, which could also account for the formation of **6f** from **1f**, is suggested in Scheme 6. The structure of compound **6f** was confirmed by independent synthesis starting from isatoic anhydride as shown in Scheme 7.

In conclusion, we have reported the synthesis of pyrrolo[2,3-*c*]quinoline-2,4(3a*H*,5*H*)-diones, based on intra- and intermolecular Wittig olefination of 3-aminoquinoline-2,4(1*H*,3*H*)-diones. The yields of the products are diminished due to relatively high reactivity of the intermediates employed in the reaction sequences, as well as the instability of final pyrrolo[2,3-*c*]quinoline-2,4(3a*H*,5*H*)-diones. The latter, for example, rearrange to the isomeric pyrrolo[3,4-*c*]quinoline-3,4(2*H*,5*H*)-diones. The reactivity of pyrrolo[2,3-*c*]quinoline-2,4(3a*H*,5*H*)-diones will be the subject of forthcoming investigations.

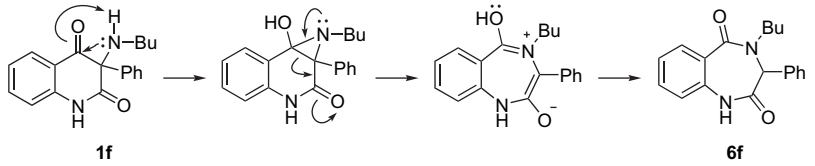
3. Experimental

3.1. General considerations

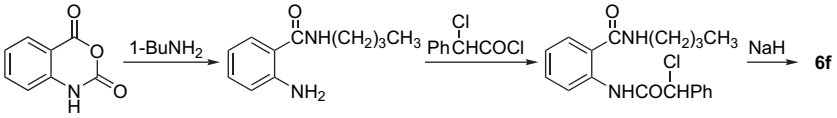
The melting points were determined on a Kofler block or Gallenkamp apparatus and are uncorrected. The IR spectra were recorded on a Perkin–Elmer 421 and 1310 and Mattson 3000 spectrophotometers using samples in potassium bromide disks. NMR data were collected on a Bruker Avance DPX 300 spectrometer operating at frequencies 300 MHz (^1H), 75 MHz



Scheme 5.



Scheme 6.



Scheme 7.

(^{13}C), and 121 MHz (^{31}P) and equipped with a 5-mm ^{1}H/^{13}C/^{31}P/^{19}F-QNP probehead or 5-mm inverse-detection probe with *z*-gradient coil for 2D experiments. Spectra were recorded at 302 K (unless otherwise indicated). Chemical shifts are given on the δ scale (parts per million) and are referenced to internal Me_4Si (^{13}C and ^{1}H) and external neat H_3PO_4 (^{31}P). Some ^{13}C chemical shifts are referenced to DMSO-d_6. Coupling constants (*J*) are given in hertz. Multiplicities are indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or br (broadened). The numbering used for the assignment of NMR signals is as follows: quinolinone skeleton (in **2** and **7**–**9**), pyrroloquinolinedione skeleton (in **3**, **4f**, **5e**, and **5f**), and benzodiazepinedione skeleton (in **6f**), simple figures; phenyl ring, primed figures; phenyl ring of triphenylphosphonium group, double primed figures. Structural elucidation and complete assignments of proton and carbon resonances of compounds **2i**, **3f**, **4f**, **5e**, **6f**, **8a**, and **9j** were performed by 2D NMR (^{1}H–^{1}H gs-COSY, ^{1}H–^{13}C gs-HSQC, gs-HMQC, and gs-HMBC) spectral analyses. In the ^{1}H spectra of other compounds, proton resonances of the fused benzene ring were tentatively assigned on the basis with analogy to **2i**, **3f**, **8a**, and **9j**, as well as our previous experiences on quinolinedione derivatives.[1–5] The mass spectra and high-resolution mass spectra were obtained with a VG-Analytical AutospecQ instrument and Q-TOF Premier instrument. Data are reported as *m*/*z* (relative intensity). Column chromatography was carried out on Silica gel 60, particle size 0.063–0.2 mm, 70–230 mesh ASTM (Fluka). The course of separation and also the purity of substances were monitored by TLC on AlugramR SIL G/UV254 foils (Macherey–Nagel). Elemental analyses (C, H, N) were performed with an Elemental Analyzer (Fisons Instrument). Solvents and reagents were used as obtained from the commercial sources. 3-Aminoquinoline-2,4(1*H*,3*H*)-diones (**1a**–**k**) were prepared according to the literature procedures.[2]

*3.2. Reaction of 3-aminoquinoline-2,4(1H,3H)-diones (**1**) with ethyl (triphenylphosphoranylidene)acetate*

A mixture of the appropriate 3-aminoquinoline-2,4(1*H*,3*H*)-dione **1** (5 mmol) and ethyl (triphenylphosphoranylidene)acetate (1.9 g, 5.5 mmol) was heated in the solvent (8 mL) at reflux and for the time indicated in Table 1. After cooling, the crude reaction mixture was column chromatographed using benzene and then successive mixtures of benzene/ethyl acetate (in ratios from 99:1 to 8:2) as eluents to give products **2**, **3**, **4f**, **5e**,**f**, **6f**, and unreacted starting material **1** (compound **2k** was oily and was transformed to its hydrochloride with hydrochloric acid). For the yields see Table 1. For physical and spectroscopic data for compounds **2**, **3**, **4f**, **5e**,**f**, and **6f** see below.

*3.3. Physical and spectroscopic data for (E)-4-ethoxycarbonylmethylene-3-amino-1,2,3,4-tetrahydroquinoline-2-ones (**2**)*

*3.3.1. (E)-Ethyl 2-(3-amino-3-butyl-2-oxo-2,3-dihydroquinolin-4(1H)-ylidene)acetate (**2a**)*

White solid, mp 103–106 °C (cyclohexane); R_f=0.15 (33% acetone in hexane); IR 3374, 3265, 3057, 2956, 2928, 2859, 1700, 1682, 1632, 1612, 1588, 1480, 1373, 1334, 1312, 1235, 1114, 1035, 1021, 920, 873, 844, 763, 751, 685 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.72 (3H, t, *J* 7.1 Hz, CH_3), 1.00–1.42 (6H, m), 1.15 (3H, t, *J* 7.1 Hz, CH_3 of ethyl), 2.03 (2H, br s, NH_2), 4.08 (2H, q, *J* 7.1 Hz, CH_2 of ethyl), 6.40 (1H, s, =CH), 6.92 (1H, d, *J* 7.6 Hz, H-8), 6.96 (1H, ddd, *J* 7.6, 7.6,

0.9 Hz, H-6), 7.30 (1H, ddd, *J* 7.6, 7.6, 1.3 Hz, H-7), 7.36 (1H, dd, *J* 7.7, 0.9 Hz, H-5), 10.40 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 13.7, 13.8, 21.9, 24.8, 38.2, 59.8, 61.7, 115.0, 116.4, 119.7, 121.6, 129.1, 130.4, 136.1, 150.0, 166.4, 173.1. Anal. Calcd for $C_{17}H_{22}N_2O_3$: C, 67.53; H, 7.33; N, 9.26. Found: C, 67.56; H, 7.28; N, 9.12.

*3.3.2. (E)-Ethyl 2-(3-butyl-3-(butylamino)-2-oxo-2,3-dihydroquinolin-4(1H)-ylidene)acetate (**2b**)*

White solid, mp 95–99 °C (hexane); R_f=0.39 (20% EtOAc in benzene); IR 3357, 3218, 3075, 2957, 2931, 2870, 1720, 1680, 1620, 1587, 1482, 1465, 1374, 1330, 1248, 1201, 1184, 1161, 773, 757, 689, 661 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.73 (3H, t, *J* 7.0 Hz, CH_3), 0.87 (3H, t, *J* 7.1 Hz, CH_3), 1.00–1.55 (11H, m, 5×CH_2, NH), 1.16 (3H, t, *J* 7.1 Hz, CH_3 of ethyl), 2.16–2.42 (2H, m), 4.12 (2H, q, *J* 7.1 Hz, CH_2 of ethyl), 6.33 (1H, s, =CH), 6.84–6.88 (2H, m, H-6 and H-8), 7.28 (1H, ddd, *J* 7.7, 7.7, 1.3 Hz, H-7), 7.35 (1H, dd, *J* 7.8, 0.9 Hz, H-5), 10.40 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 13.68, 13.78, 13.82, 19.8, 22.0, 24.4, 32.4, 38.5, 42.2, 60.0, 67.0, 115.1, 118.0, 118.8, 121.6, 129.2, 130.6, 136.2, 145.7, 167.2, 171.4. Anal. Calcd for $C_{21}H_{30}N_2O_3$: C, 70.36; H, 8.44; N, 7.81. Found: C, 70.14; H, 8.46; N, 8.07.

*3.3.3. (E)-Ethyl 2-(3-amino-3-benzyl-2-oxo-2,3-dihydroquinolin-4(1H)-ylidene)acetate (**2c**)*

White solid, mp 202–204 °C (benzene/cyclohexane); R_f=0.40 (33% hexane in EtOAc); IR 3377, 3333, 3050, 3031, 2991, 1694, 1686, 1623, 1585, 1482, 1459, 1376, 1312, 1272, 1214, 1178, 1038, 1031, 891, 864, 836, 811, 764, 710, 700, 690, 645 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.11 (3H, t, *J* 7.0 Hz, CH_3), 2.00 (2H, br s, NH_2), 2.65 and 2.72 (2H, 2d, *J* 13.0 Hz, CH_2 of benzyl), 4.05 (2H, q, *J* 7.0 Hz, CH_2 of ethyl), 6.12 (1H, s, =CH), 6.90–7.27 (7H, m, H-6, H-8 and phenyl), 7.36 (1H, m, H-7), 7.42 (1H, d, *J* 7.6 Hz, H-5), 10.58 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 13.7, 44.4, 59.8, 62.5, 115.3, 117.3, 119.8, 121.8, 126.6, 127.5, 129.5, 130.2, 130.5, 135.0, 136.1, 148.9, 166.3, 171.9. Anal. Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33. Found: C, 71.52; H, 5.76; N, 8.28.

*3.3.4. (E)-Ethyl 2-(3-amino-2-oxo-3-phenyl-2,3-dihydroquinolin-4(1H)-ylidene)acetate (**2e**)*

Off-white solid, mp 155–160 °C (benzene/ethyl acetate); R_f=0.51 (5% ethanol in chloroform); IR 3370, 3303, 3284, 3193, 3084, 3058, 2982, 2914, 2869, 1713, 1686, 1648, 1613, 1586, 1577, 1491, 1482, 1450, 1437, 1368, 1339, 1280, 1250, 1221, 1188, 1158, 1106, 1024, 1009, 947, 922, 886, 869, 850, 771, 748, 701, 683, 655 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.17 (3H, t, *J* 6.9 Hz, CH_3), 2.57 (2H, br s, NH_2), 4.12 (2H, q, *J* 6.9 Hz, CH_2), 6.80 (1H, s, =CH_2), 6.80–7.38 (9H, m), 10.71 (1H, br s, H-1); δ_C (75 MHz, DMSO-d_6) 13.9, 60.1, 65.2, 115.2, 117.9, 120.7, 121.8, 125.8, 127.5, 128.4, 129.2, 130.2, 135.6, 142.0, 149.2, 166.5, 171.4; EIMS *m/z* (%) 322 (M^+, 10), 305 (14), 276 (40), 249 (100), 221 (33), 104 (30); HREI-MS calcd for $C_{19}H_{18}N_2O_3$ 322.1317, found 322.1320.

*3.3.5. (E)-Ethyl 2-(3-amino-1-methyl-2-oxo-3-phenyl-2,3-dihydroquinolin-4(1H)-ylidene)acetate (**2g**)*

White solid, mp 96–105 °C (cyclohexane); R_f=0.55 (10% ethanol in chloroform); IR 3366, 3043, 2980, 2936, 1720, 1682, 1640, 1601, 1491, 1468, 1448, 1367, 1363, 1256, 1217, 1158, 1040, 854, 834, 754, 702 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.17 (3H, t, *J* 7.1 Hz, CH_3 of ethyl), 3.40 (3H, s, CH_3), 4.12 (2H, q, *J* 7.1 Hz, CH_2 of ethyl), 6.78 (1H, s, =CH), 6.93 (1H, ddd, *J* 7.5, 7.5, 0.8 Hz, H-6), 7.02–7.22 (6H, m, C_6H_5 and H-8), 7.25 (1H, ddd, *J* 7.6, 7.6, 1.4 Hz, H-7), 7.32 (1H, dd, *J* 7.6, 1.4 Hz, H-5); δ_C (75 MHz, DMSO-d_6) 13.8, 30.4, 60.0, 65.8, 114.9, 117.4, 122.29, 122.33, 125.6, 127.5, 128.3, 129.3, 130.3, 137.5, 141.8, 149.3, 166.1, 170.8; FABMS *m/z* (%) 337 (M^++1, 100), 320 (84), 247 (44), 105 (45). Anal. Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33. Found: C, 71.21; H, 6.15; N, 8.28.

*3.3.6. (E)-Ethyl 2-(3-(butylamino)-1-methyl-2-oxo-3-phenyl-2,3-dihydroquinolin-4(1H)-ylidene)acetate (**2h**)*

Yellow oil; R_f=0.40 (33% EtOAc in hexane); IR 3332, 2956, 2928, 2870, 1720, 1677, 1637, 1601, 1493, 1462, 1446, 1359, 1271, 1210, 1161, 1041, 1033, 940, 850, 753, 702 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.81 (3H, t, *J* 7.2 Hz, CH_3), 1.16 (3H, t, *J* 7.1 Hz, CH_3 of ethyl), 1.27 (2H, m), 1.38 (2H, m), 2.23 (2H, m), 2.62 (1H, br t, *J* 7.1 Hz, NH), 3.37 (3H, s, CH_3), 4.12 (2H, q, *J* 7.1 Hz, CH_2 of ethyl), 6.65 (1H, s, =CH), 6.94 (1H, ddd, *J* 7.5, 7.5, 0.5 Hz, H-6), 7.03–7.28 (7H, m), 7.36 (1H, dd, *J* 7.6, 1.4 Hz, H-5); δ_C (75 MHz, DMSO-d_6) 13.7, 13.8, 19.7, 30.2, 32.2, 43.2, 60.1, 70.0, 114.9, 118.4, 122.1, 122.4, 126.9, 127.6, 128.2, 129.5, 130.3, 137.2, 138.6, 147.4, 166.2, 169.5; EIMS *m/z* (%) 392 (M^+, 7), 346 (27), 319 (100), 104 (50); HREI-MS calcd for $C_{24}H_{28}N_2O_3$ 392.2100, found 392.2089.

*3.3.7. (E)-Ethyl 2-(3-amino-3-methyl-2-oxo-1-phenyl-2,3-dihydroquinolin-4(1H)-ylidene)acetate (**2i**)*

Yellowish solid; mp 148–152 °C (cyclohexane); R_f=0.71 (10% ethanol in chloroform); IR 3369, 3312, 3070, 2986, 2965, 2924, 2901, 2853, 1719, 1686, 1636, 1601, 1498, 1461, 1456, 1376, 1366, 1329, 1303, 1272, 1225, 1201, 1168, 1032, 931, 910, 886, 863, 767, 751, 703, 520, 491 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.19 (3H, t, *J* 7.1 Hz, CH_3 of ethyl), 1.32 (3H, s, CH_3), 2.82 (2H, br s, NH_2), 4.13 (2H, q, *J* 7.1 Hz, CH_2), 6.27 (1H, d, *J* 7.9 Hz, H-8), 6.56 (1H, s, =CH), 7.05 (1H, ddd, *J* 7.5, 7.5, 0.9 Hz, H-6), 7.20–7.26 (3H, m, H-7, H-2′, H-6′), 7.44–7.52 (2H, m, H-5, H-4′), 7.52–7.60 (2H, m, H-3′, H-5′); δ_C (75 MHz, DMSO-d_6) 13.8 (CH_3CH_2), 26.9 (CH_3), 59.1 (C-3), 59.9 (CH_2), 115.6 (=CH), 115.9 (C-8), 121.0 (C-4a), 122.4 (C-6), 128.3, 128.7, 129.5 (C-5), 129.9, 130.2, 137.9 (C-1′), 138.7 (C-8a), 150.5 (C-4), 166.2 (COO), 173.0 (C-2). Anal. Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33. Found: C, 71.16; H, 6.29; N, 8.25.

*3.3.8. (E)-Ethyl 2-(3-(butylamino)-3-methyl-2-oxo-1-phenyl-2,3-dihydroquinolin-4(1H)-ylidene)acetate (**2j**)*

Yellowish solid; mp 85–91 °C (hexane); R_f=0.60 (10% ethanol in chloroform); IR 3062, 3041, 2967, 2958, 2933, 2871, 1721, 1678, 1638, 1599, 1492, 1456, 1370, 1351, 1322, 1301, 1266, 1253, 1216, 1201, 1182, 1169, 1165, 1147, 1122, 1092,

1073, 1027, 974, 943, 871, 835, 775, 766, 759, 751, 699, 684, 666, 631, 542, 524, 513, 506, 482, 459, 416 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.84 (3H, t, *J* 7.0 Hz, CH_3), 1.19 (3H, t, *J* 7.0 Hz, CH_3 of ethyl), 1.22–1.39 (4H, m), 1.39 (3H, s, CH_3), 2.37–2.50 (3H, m, $NHCH_2$), 4.15 (2H, q, *J* 7.0 Hz, CH_2 of ethyl), 6.22 (1H, d, *J* 8.14 Hz, H-8), 6.44 (1H, s, =CH), 7.02 (1H, dd, *J* 7.5, 7.5 Hz), 7.18–7.26 (3H, m), 7.45–7.60 (4H, m); δ_C (75 MHz, DMSO-d_6) 13.78, 13.80, 19.7, 24.9, 32.3, 42.3, 60.1, 63.8, 115.7, 117.1, 120.2, 122.3, 128.3, 128.9, 129.7, 129.9, 130.3, 137.8, 138.7, 147.8, 166.7, 170.8; EIMS *m/z* (%) 392 (M^+, 3), 346 (31), 319 (100). Anal. Calcd for $C_{24}H_{28}N_2O_3$: C, 73.44; H, 7.19; N, 7.14. Found: C, 73.10; H, 6.91; N, 7.18.

*3.3.9. (E)-Ethyl 2-(1-benzyl-3-(butylamino)-2-oxo-3-phenyl-2,3-dihydroquinolin-4(1H)-ylidene)acetate hydrochloride (**2k**·HCl)*

White solid; mp 172–178 °C (ethanol); IR 3432 (br), 3060, 3032, 2962, 2935, 2873, 2460–2830, 2533, 2421, 2384, 1728, 1686, 1639, 1602, 1495, 1466, 1450, 1382, 1312, 1275, 1225, 1186, 1100, 1029, 992, 862, 771, 725, 695, 609, 548 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.83 (3H, t, *J* 7.1 Hz), 1.13 (3H, t, *J* 7.0 Hz), 1.19–1.33 (2H, m), 1.76 (2H, m), 3.04 (1H, br s), 3.70 (1H, br s), 4.13 (2H, m), 5.33 (2H, m), 6.93–7.40 (15H, m), 10.09 (1H, br s), 11.11 (1H, br s). Anal. Calcd for $C_{30}H_{33}ClN_2O_3$: C, 71.34; H, 6.59; N, 5.55. Found: C, 71.73; H, 6.73; N, 5.58.

Because of low solubility of **2k**·HCl, the compound was for ^{13}C NMR measurement freebased by extraction from saturated aqueous solution of $NaHCO_3$ into dichloromethane. Compound **2k**: δ_C (75 MHz, $CDCl_3$) 13.95, 14.04, 20.3, 32.8, 43.7, 47.9, 60.5, 70.5, 115.4, 119.9, 122.8, 123.6, 126.3, 127.1, 127.8, 128.03, 128.11, 129.0, 129.9, 130.1, 136.6, 137.2, 138.1, 148.0, 167.0, 170.5.

*3.4. Physical and spectroscopic data for pyrrolo[2,3-c]-quinoline-2,4(5H)-diones **3***

*3.4.1. 3a-Butyl-3,3a-dihydro-2H-pyrrolo[2,3-c]quinoline-2,4(5H)-dione (**3a**)*

White solid; mp 265–269 °C (diethyl ether); R_f=0.50 (10% ethanol in chloroform); IR 3265, 3144, 3082, 2957, 2932, 1746, 1692, 1676, 1607, 1526, 1477, 1456, 1360, 1300, 1289, 1248, 1172, 962, 872, 823, 760, 744, 642 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.75 (3H, t, *J* 6.8 Hz, CH_3), 1.00–1.20 (4H, m), 1.40–1.52 and 1.77–1.88 (2H, 2m), 6.21 (1H, d, *J* 1.2 Hz, H-1), 7.03 (1H, d, *J* 8.0 Hz, H-8), 7.11 (1H, ddd, *J* 7.5, 7.5, 0.6 Hz, H-6), 7.39 (1H, ddd, *J* 7.8, 7.8, 1.3 Hz, H-7), 7.62 (1H, dd, *J* 7.6, 1.0 Hz, H-5), 8.72 (1H, br s, NH), 10.44 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 13.6, 21.7, 24.3, 37.1, 67.8, 115.7, 116.5, 119.5, 122.9, 126.3, 131.4, 137.1, 155.8, 169.5, 171.8; HRESI-MS calcd for $C_{15}H_{17}N_2O_2$ $[M+1]^+$ 257.1290, found 257.1295.

*3.4.2. 3,3a-Dibutyl-3,3a-dihydro-2H-pyrrolo[2,3-c]-quinoline-2,4(5H)-dione (**3b**)*

White solid; mp 186–190 °C (benzene/cyclohexane); R_f=0.51 (20% EtOAc in benzene); IR 3225, 3126, 3081, 2956, 2930, 2870, 1707, 1661, 1608, 1478, 1468, 1399, 1363, 1344, 1298, 1128, 1032, 867, 851, 760, 750, 6471 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.71 (3H, t, *J* 7.5 Hz, CH_3), 0.70–0.84 (2H, m), 0.93 (3H, t, *J* 7.4 Hz, CH_3), 1.04–1.20 (2H, m), 1.28–1.40 (2H, m), 1.54–1.83 (3H, m), 2.03–2.17 (1H, m), 3.25–3.55 (2H, m), 6.38 (1H, s, H-1), 7.05 (1H, d, *J* 8.0 Hz, H-8), 7.12 (1H, dd, *J* 7.5, 7.5 Hz, H-6), 7.40 (1H, dd, *J* 7.1, 7.1 Hz, H-7), 7.63 (1H, d, *J* 7.1 Hz, H-5), 10.49 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 13.6, 13.8, 20.0, 21.3, 23.4, 30.6, 33.9, 41.2, 70.4, 115.7, 116.4, 119.8, 123.1, 126.2, 131.4, 136.7, 153.6, 169.6, 170.4; EIMS *m/z* (%) 312 (M^+, 89), 296 (100), 266 (97), 213 (97), 199 (51), 185 (59); HREI-MS calcd for $C_{19}H_{24}N_2O_2$ 312.1838, found 312.1846.

*3.4.3. 3a-Benzyl-3,3a-dihydro-2H-pyrrolo[2,3-c]quinoline-2,4(5H)-dione (**3c**)*

White solid; mp 315–322 °C (AcOH); R_f=0.48 (10% ethanol in chloroform); IR 3257, 3058, 2977, 2909, 2872, 1692, 1667, 1622, 1606, 1585, 1481, 1437, 1370, 1244, 1228, 1144, 1112, 1036, 969, 871, 779, 745, 683, 636 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 2.84 and 3.10 (2H, 2d, *J* 13.1 Hz, CH_2), 5.91 (1H, d, *J* 1.0 Hz, H-1), 6.88–6.95 (2H, m), 7.09 (1H, d, *J* 7.9 Hz, H-6), 7.15–7.22 (4H, m), 7.45 (1H, ddd, *J* 7.5, 7.5, 1.2 Hz, H-7), 7.53 (1H, dd, *J* 7.5, 1.2 Hz, H-9), 8.81 (1H, br s, NH), 10.59 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 42.5, 68.2, 116.0, 116.9, 120.6, 123.3, 126.3, 126.9, 127.4, 130.4, 131.4, 132.8, 137.0. Anal. Calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.27; H, 4.77; N, 9.43.

*3.4.4. 3a-Benzyl-3-butyl-3,3a-dihydro-2H-pyrrolo[2,3-c]-quinoline-2,4(5H)-dione (**3d**)*

White solid; mp 220–223 °C (benzene/cyclohexane); R_f=0.70 (10% ethanol in chloroform); IR 3028, 2965, 2924, 2862, 1693, 1656, 1605, 1495, 1479, 1358, 1344, 1295, 1157, 1104, 1031, 879, 852, 759, 699, 635 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.95 (3H, t, *J* 7.3 Hz, CH_3), 1.30–1.45 (2H, m), 1.69–1.86 (2H, m), 2.87 and 3.45 (2H, 2d, *J* 13.6 Hz, CH_2Ph), 3.40–3.51 and 3.55–3.68 (2H, 2m), 6.12 (1H, s, H-1), 6.76–6.83 (2H, m), 7.10 (1H, d, *J* 8.0 Hz, H-6), 7.15–7.23 (4H, m), 7.44 (1H, ddd, *J* 7.5, 7.5, 0.9 Hz, H-7), 7.58 (1H, dd, *J* 7.2, 0.5 Hz, H-9), 10.62 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 13.8, 20.0, 31.1, 42.0, 71.2, 115.9, 116.7, 120.3, 123.3, 126.1, 127.1, 127.6, 128.2, 129.8, 131.4, 132.4, 136.7, 152.8, 168.8, 169.6. Anal. Calcd for $C_{22}H_{22}N_2O_2$: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.41; H, 6.37; N, 7.91.

*3.4.5. 3a-Phenyl-3,3a-dihydro-2H-pyrrolo[2,3-c]quinoline-2,4(5H)-dione (**3e**)*

White solid; mp 268–278 °C (acetic acid); R_f=0.67 (10% ethanol in chloroform); IR 3282, 3147, 3085, 3056, 2988, 2973, 2926, 2909, 2871, 1703, 1697, 1693, 1671, 1668, 1627, 1608, 1479, 1450, 1357, 1301, 1244, 1229, 1158, 1107, 1088, 1033, 975, 946, 915, 869, 833, 782, 751, 714, 695, 683, 643, 567, 494, 464, 431 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 6.44 (1H, d, *J* 1.0 Hz, H-1), 6.95 (1H, d, *J* 8.0 Hz, H-6), 7.08 (1H, ddd, *J* 7.5, 7.5, 0.7 Hz, H-8), 7.20–7.39 (6H, m), 7.66 (1H, dd, *J* 7.5,

1.0 Hz, H-9), 9.25 (1H, br s, NH), 10.73 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 70.0, 115.8, 117.5, 120.9, 123.2, 125.5, 126.4, 128.6, 128.9, 131.5, 136.8, 137.3, 155.7, 168.0, 171.6. Anal. Calcd for $C_{17}H_{12}N_2O_2$: C, 73.90; H, 4.38; N, 10.14. Found: C, 74.18; H, 4.62; N, 9.90.

*3.4.6. 3-Butyl-3a-phenyl-3,3a-dihydro-2H-pyrrolo[2,3-c]-quinoline-2,4(5H)-dione (**3f**)*

White solid; mp 195–202 °C (xylene); R_f=0.46 (10% ethanol in chloroform); IR 3211, 3183, 3168, 3117, 3072, 3029, 2963, 2918, 2872, 2858, 1703, 1660, 1609, 1587, 1478, 1447, 1392, 1362, 1339, 1287, 1233, 1190, 1109, 1092, 1077, 1034, 1003, 944, 923, 899, 886, 784, 753, 714, 696, 640, 590, 570, 542, 524, 493, 469, 450 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.72 (3H, t, J 7.2 Hz, CH_3), 0.95–1.14 (2H, m, CH_3CH_2), 0.95–1.14 and 1.35–1.50 (2H, m, $CH_3CH_2CH_2$), 3.05–3.15 and 3.30–3.40 (2H, m, $CH_3CH_2CH_2CH_2$), 6.60 (1H, s, H-1), 6.93 (1H, d, J 7.8 Hz, H-6), 7.04 (1H, dd, J 7.8, 7.8 Hz, H-8), 7.18–7.23 (2H, m, H-2′, H-6′), 7.29 (1H, dd, J 7.8, 7.8 Hz, H-7), 7.30–7.42 (3H, m, H-3′, H-4′, H-5’), 7.61 (1H, d, J 7.8 Hz, H-9), 10.83 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 14.5 (CH_3), 20.6 (CH_3CH_2), 30.8 ($CH_3CH_2CH_2$), 42.8 ($CH_3CH_2CH_2CH_2$), 73.9 (C-3a), 116.6 (C-6), 118.3 (C-9a), 121.6 (C-1), 124.1 (C-8), 127.0 (C-2’, C-6′), 127.3 (C-9), 130.07 (C-4′), 130.14 (C-3′, C-5′), 132.3 (C-7), 135.6 (C-1′), 137.2 (C-5a), 155.4 (C-9b), 168.9 (C-4), 171.1 (C-2); EIMS *m/z* (%) 332 (M^+, 100), 289 (62), 261 (39), 233 (29), 204 (23), 91 (36). Anal. Calcd for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.06; N, 8.43. Found: C, 75.84; H, 5.90; N, 8.43.

*3.4.7. 5-Methyl-3a-phenyl-3,3a-dihydro-2H-pyrrolo[2,3-c]-quinoline-2,4(5H)-dione (**3g**)*

White solid; mp 250–255 °C (benzene); R_f=0.30 (33% hexane in EtOAc); IR 3168, 3079, 3058, 2971, 2800, 1688, 1663, 1648, 1603, 1490, 1468, 1447, 1352, 1308, 1279, 1177, 1132, 1093, 1043, 949, 882, 760, 748, 698, 688, 650 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 3.38 (3H, s, CH_3), 6.46 (1H, s, H-1), 7.05–7.35 (7H, m), 7.43 (1H, dd, J 7.5, 7.5 Hz, H-7), 7.69 (1H, d, J 7.2 Hz, H-9), 9.32 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 30.0, 69.8, 115.8, 118.8, 120.6, 123.5, 125.4, 126.4, 128.6, 128.8, 131.5, 137.0, 138.3, 154.9, 167.3, 171.4. Anal. Calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.11; H, 4.84; N, 9.36.

*3.4.8. 3-Butyl-5-methyl-3a-phenyl-3,3a-dihydro-2H-pyrrolo[2,3-c]quinoline-2,4(5H)-dione (**3h**)*

White solid; mp 142–144 °C (cyclohexane); R_f=0.70 (33% hexane in EtOAc); IR 3084, 2956, 2932, 2870, 1692, 1647, 1601, 1582, 1491, 1467, 1453, 1353, 1324, 1279, 1134, 1098, 1045, 960, 916, 857, 849, 748, 698, 635 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.72 (3H, t, J 7.0 Hz, CH_3), 0.97–1.17 (3H, m), 1.38–1.55 (1H, m), 3.03–3.18 and 3.27–3.42 (2H, 2m), 3.41 (3H, s, NCH_3), 6.63 (1H, s, H-1), 7.05–7.17 (3H, m), 7.21 (1H, d, J 8.2 Hz, H-6), 7.28–7.37 (3H, m), 7.40 (1H, ddd, J 7.8, 7.8, 1.3 Hz, H-7), 7.65 (1H, dd, J 7.5, 1.1 Hz, H-9); δ_C (75 MHz, DMSO-d_6) 13.5, 19.7, 29.9, 41.9, 73.0, 115.8, 118.6, 120.3, 123.5, 125.9, 126.4, 129.1, 129.2, 131.4, 134.6, 137.9, 153.7, 167.2, 170.2; HRESI-MS calcd for $C_{22}H_{23}N_2O_2$ $[M+1]^+$ 347.1760, found 347.1771.

*3.4.9. 3a-Methyl-5-phenyl-3,3a-dihydro-2H-pyrrolo[2,3-c]-quinoline-2,4(5H)-dione (**3i**)*

White solid; mp 297–299 °C (AcOH); R_f=0.56 (10% ethanol in chloroform); IR 3339, 3259, 3089, 3065, 2984, 1701, 1692, 1632, 1597, 1492, 1479, 1459, 1370, 1342, 1314, 1279, 1204, 1160, 1135, 970, 931, 858, 765, 754, 740, 709, 642, 585, 504, 444 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.56 (3H, s, CH_3), 6.32 (1H, d, J 8.9 Hz, H-6), 6.33 (1H, s, H-1), 7.20 (2H, dd, J 7.4, 7.2 Hz), 7.29–7.37 (2H, m), 7.47–7.58 (3H, m), 7.76 (1H, dd, J 6.5, 0.9 Hz, H-9), 8.92 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 25.9, 64.8, 116.6, 117.3, 119.0, 123.5, 126.9, 128.7, 129.1 (br), 130.1 (br), 131.3, 137.6, 139.6, 156.4, 169.2, 171.3. Anal. Calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.32; H, 5.08; N, 9.60.

*3.4.10. 3-Butyl-3a-methyl-5-phenyl-3,3a-dihydro-2H-pyrrolo[2,3-c]quinoline-2,4(5H)-dione (**3j**)*

White solid; mp 145–147 °C (benzene/cyclohexane); R_f=0.26 (20% EtOAc in benzene); IR 3068, 3048, 2991, 2974, 2957, 2934, 2908, 2870, 2854, 1698, 1687, 1635, 1600, 1492, 1481, 1459, 1430, 1392, 1367, 1358, 1339, 1315, 1290, 1281, 1260, 1247, 1207, 1186, 1159, 1146, 1134, 1120, 1100, 1071, 1042, 1025, 1001, 976, 967, 948, 914, 858, 764, 732, 707, 678, 640, 633, 593, 507, 481, 433 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.90 (3H, t, J 6.8 Hz, CH_3), 1.23–1.38 (2H, m), 1.63 (3H, s, CH_3), 1.63–1.80 (2H, m), 3.36–3.63 (2H, m), 6.32 (1H, d, J 7.9 Hz, H-6), 6.49 (1H, s, H-1), 7.26–7.30 (2H, m), 7.30–7.46 (2H, m), 7.46–7.63 (3H, m), 7.77 (1H, d, J 7.0 Hz, H-9); δ_C (75 MHz, DMSO-d_6) 13.7, 19.9, 24.0, 30.7, 41.3, 67.4, 116.6, 117.2, 118.9, 123.6, 126.7, 128.7, 129.4 (br), 130.0 (br), 131.2, 137.4, 139.2, 154.9, 169.1, 169.7; δ_C (75 MHz, DMSO-d_6, 343 K) 13.6, 20.0, 24.0, 30.7, 41.4, 67.5, 116.6, 117.4, 118.9, 123.6, 126.7, 128.6, 129.0, 130.0, 131.2, 137.5, 139.3, 155.0, 169.2, 169.7; EIMS *m/z* (%) 346 (M^+, 100), 303 (59), 289 (45), 275 (35), 77 (19). Anal. Calcd for $C_{22}H_{22}N_2O_2$: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.11; H, 6.29; N, 8.06.

*3.4.11. 2-Butyl-1-phenyl-1H-pyrrolo[3,4-c]quinoline-3,4-(2H,5H)-dione (**4f**)*

White solid; mp 252–260 °C; R_f=0.45 (10% ethanol in chloroform); IR 3404 (br), 3143, 3100, 3066, 3027, 3008, 2952, 2931, 2872, 1703, 1648, 1621, 1604, 1562, 1511, 1480, 1455, 1438, 1415, 1393, 1366, 1325, 1313, 1279, 1269, 1253, 1220, 1196, 1188, 1156, 1079, 1032, 953, 895, 859, 803, 774, 757, 714, 699, 649, 644, 595, 557, 530, 518, 495, 462, 433 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.82 (3H, t, J 7.3 Hz, CH_3), 1.12–1.25 (2H, m, CH_3CH_2), 1.33–1.46 (2H, m, $CH_3CH_2CH_2$), 2.58–2.70 and 3.55–3.66 (2H, 2m, $CH_3CH_2CH_2CH_2$), 6.08 (1H, s, H-1), 7.05 (1H, ddd, J 8.1, 8.1, 1.0 Hz, H-8), 7.32 (1H, dd, J 8.1, 1.0 Hz, H-9), 7.33–7.44 (6H, m, H-6, Ph), 7.52 (1H, ddd, J 7.1, 8.1,

1.0 Hz, H-7), 11.96 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 13.4 (CH_3), 19.2 (CH_3CH_2), 29.6 ($CH_3CH_2CH_2$), 38.9 ($CH_3CH_2CH_2CH_2$), 61.1 (C-1), 114.2 (C-9a), 115.9 (C-6), 120.4 (C-3a), 121.8 (C-8), 124.6 (C-9), 127.9 (Ph), 128.8 (Ph), 129.2 (Ph), 132.1 (C-7), 136.0 (C-1′), 140.7 (C-5a), 156.9 (C-4), 159.3 (C-9b), 164.9 (C-3); EIMS *m/z* (%) 332 (M^+, 46), 289 (24), 261 (39), 95 (100); HRESI-MS calcd for $C_{21}H_{21}N_2O_2$ $[M+1]^+$ 333.1603, found 333.1612.

3.4.12. 1-Hydroxy-1-phenyl-1H-pyrrolo[3,4-c]quinoline-3,4(2H,5H)-dione (**5e**)

Yellow solid; mp 298–302 °C (acetic acid); R_f=0.13 (10% ethanol in chloroform); IR 3404, 3301, 3189, 3096, 3067, 2919, 2850, 1754, 1728, 1682, 1650, 1619, 1561, 1468, 1452, 1434, 1410, 1385, 1332, 1267, 1200, 1176, 1157, 1137, 1068, 1033, 1006, 946, 931, 894, 846, 810, 779, 760, 748, 724, 699, 602, 556, 532, 516, 491, 462 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 7.06 (1H, dd, *J* 7.5, 7.5 Hz, H-8), 7.26 (1H, br s, OH), 7.28–7.41 (4H, m, H-6, H-3′, H-4′, H-5′), 7.47–7.57 (4H, m, H-7, H-9, H-2′, H-6′), 9.11 (1H, br s, H-2), 11.97 (1H, br s, H-5); δ_C (75 MHz, DMSO-d_6) 85.7, 113.5 (C-9a), 115.9 (C-6), 119.0 (C-3a), 121.8 (C-8), 125.4, 125.7, 128.1, 128.4, 132.3, 140.4, 141.7, 157.2, 162.1, 166.0; EIMS *m/z* (%) 292 (M^+, 50), 263 (62), 215 (75), 105 (75), 77 (100); HREI-MS calcd for $C_{17}H_{12}N_2O_3$ 292.0848, found 292.0846.

3.4.13. 2-Butyl-1-hydroxy-1-phenyl-1H-pyrrolo[3,4-c]-quinoline-3,4(2H,5H)-dione (**5f**)

White solid; mp 212–220 °C (benzene/hexane); R_f=0.15 (10% ethanol in chloroform); IR 3148, 3059, 2960, 2931, 2871, 1721, 1650, 1566, 1484, 1439, 1415, 1371, 1312, 1190, 1120, 1045, 927, 862, 807, 759, 752, 722, 698, 606, 542 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.73 (3H, t, *J* 7.0 Hz, CH_3), 1.06–1.33 (4H, m), 2.83–2.92 and 3.17–3.28 (2H, 2m), 7.05 (1H, ddd, *J* 7.7, 7.6, 1.0 Hz, H-8), 7.30–7.47 (8H, m), 7.52 (1H, ddd, *J* 8.2, 7.3, 1.4 Hz, H-7), 12.04 (1H, br s, OH); δ_C (75 MHz, DMSO-d_6) 13.4, 19.5, 30.3, 37.7, 88.5, 113.2, 115.9, 119.0, 121.9, 125.4, 125.5, 128.4, 128.6, 132.2, 138.6, 141.5, 156.8, 160.4, 164.9; EIMS *m/z* (%) 348 (M^+, 27), 221 (100), 77 (52). Anal. Calcd for $C_{21}H_{20}N_2O_3$: C, 72.40; H, 5.79; N, 8.04. Found: C, 72.39; H, 5.80; N, 8.05.

3.4.14. 4-Butyl-3-phenyl-3,4-dihydro-1H-benzo[e][1,4]-diazepine-2,5-dione (**6f**)

White solid; mp 159–163 °C (benzene/hexane); R_f=0.79 (10% ethanol in chloroform); IR 3206, 3085, 2956, 2926, 2869, 2860, 1676, 1633, 1606, 1583, 1496, 1484, 1462, 1450, 1434, 1416, 1401, 1364, 1317, 1304, 1295, 1278, 1250, 1221, 1196, 1155, 1113, 1079, 1046, 1032, 966, 882, 868, 843, 818, 795, 765, 735, 693, 648, 587, 540, 493, 472, 418 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.93 (3H, t, *J* 7.3 Hz, CH_3), 1.27–1.42 (2H, m, CH_3CH_2), 1.55–1.74 (2H, m, $CH_3CH_2CH_2$), 3.45–3.60 and 4.04–4.20 (2H, 2m, $CH_3CH_2CH_2CH_2$), 5.46 (1H, s, H-3), 6.83 (1H, d, *J* 8.0 Hz, H-9), 6.90 (1H, dd, *J* 7.6, 7.6 Hz, H-7), 6.94–7.01 (2H, m, H-2′, H-6′), 7.02–7.09 (1H, m, H-4′), 7.10–7.18 (2H, m, H-3′, H-5′), 7.19 (1H, dd, *J* 8.0, 8.0 Hz, H-8), 7.47 (1H, dd, *J* 7.8, 1.6 Hz, H-6), 10.67 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 13.6 (CH_3), 19.3 (CH_3CH_2), 29.8 ($CH_3CH_2CH_2$), 49.6 ($CH_3CH_2CH_2CH_2$), 66.0 (C-3), 119.8 (C-9), 123.4 (C-7), 124.1 (C-2′, C-6′), 127.17 and 127.19 (C-5a and C-4′), 128.2 (C-3′, C-5′), 130.1 (C-6), 131.5 (C-8), 134.4 (C-1′), 135.0 (C-9a), 166.0 (C-5), 170.7 (C-2); EIMS *m/z* (%) 308 (M^+, 70), 251 (27), 208 (32), 203 (100), 147 (60), 119 (52), 91 (47). Anal. Calcd for $C_{19}H_{20}N_2O_2$: C, 74.00; H, 6.54; N, 9.08. Found: C, 74.21; H, 6.74; N, 8.98.

3.4.15. Independent synthesis of **6f**

2-Amino-*N*-butylbenzamide was prepared from isatoic anhydride and butyl amine as described in the literature.[12]

To a vigorously stirred ice-cold mixture of 2-amino-*N*-butylbenzamide (384 mg, 2.0 mmol), dichloromethane (20 mL), and saturated aqueous solution of $NaHCO_3$ (20 mL), a solution of 2-chloro-2-phenylacetyl chloride (90%, 416 mg, 2.0 mmol) in dichloromethane (5 mL) was added dropwise. The reaction mixture was then stirred at room temperature for 45 min. The layers were separated and the water layer was extracted with dichloromethane (5 mL). The combined organic layers were dried over Na_2SO_4 and evaporated to dryness to give *N*-butyl-2-(2-chloro-2-phenylacetamido)benzamide (659 mg, 95%) as brown solid. For analyses, the product was crystallized from acetonitrile to give white needles. Mp 123–124 °C (acetonitrile); IR 3303, 2958, 2934, 1676, 1627, 1593, 1551, 1515, 1447, 1296, 1226, 754, 725, 699 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.91 (3H, t, *J* 7.3 Hz), 1.28–1.42 (2H, m), 1.47–1.59 (2H, m), 3.28 (2H, br q, *J* 7.3 Hz), 5.94 (1H, s), 7.21 (1H, ddd, *J* 7.6, 7.6, 0.9 Hz), 7.35–7.58 (6H, m), 7.75 (1H, dd, *J* 7.9, 1.3 Hz), 8.35 (1H, d, *J* 7.8 Hz), 8.75 (1H, br t, *J* 5.3 Hz), 12.12 (1H, br s); δ_C (75 MHz, DMSO-d_6) 13.7, 19.6, 30.9, 38.8, 61.2, 120.5, 121.9, 123.5, 127.9, 128.0, 128.7, 128.9, 131.7, 137.3, 137.8, 165.8, 167.8. Anal. Calcd for $C_{19}H_{21}ClN_2O_2$: C, 66.18; H, 6.14; N, 8.12. Found: C, 66.13; H, 5.98; N, 8.11.

A mixture of *N*-butyl-2-(2-chloro-2-phenylacetamido)benzamide (82 mg, 0.24 mmol) and NaH (60% dispersion in mineral oil, 80 mg, 2.0 mmol) in DMF (3 mL) was stirred at room temperature for 2 h. Ammonium chloride solution (5 mL, satd aq) was added and the product was extracted with ethyl acetate/hexane (3:5, 10 mL). The organic layer was separated, dried over Na_2SO_4, concentrated in vacuo, and subjected to column chromatography using ethyl acetate/hexane (3:5) as eluant to give **6f** (33 mg, 45%) as white solid, mp 158–159 °C (benzene/hexane). IR and NMR spectra are in agreement with those for **6f** obtained from **1f**, as described above.

3.5. General procedure for the synthesis of 3-bromoacetamidoquinoline-2,4(1H,3H)-diones **7a–d,f–h,j** in benzene with K_2CO_3 as a base

To a solution of 3-aminoquinoline-2,4(1*H*,3*H*)-dione **1** (**a–d,f–h,j**) (10 mmol) in benzene (60 mL), powdered potassium carbonate (4.15 g, 30 mmol) and bromoacetyl bromide

(1 mL, 11.45 mmol) were added with stirring, at room temperature. The reaction mixture was stirred for 2 h, methanol (1 mL) was added, and the solids were filtered off. The filtrate was diluted with benzene (30 mL) and consecutively washed with 3% hydrochloric acid (30 mL), water, 5% solution of potassium carbonate (30 mL), and again water (30 mL). The benzene layer was dried with anhydrous sodium sulfate, filtered, and evaporated to dryness to give crude **7** (**a**–**d**,**f**–**h**,**j**), which was crystallized from the solvent given below. For yields of analytically pure products, see Table 2. For physical and spectroscopic data, see below.

*3.5.1. 2-Bromo-N-(3-butyl-2,4-dioxo-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**7a**)*

White solid; mp 195–197 °C (ethyl acetate); IR 3351, 3189, 3058, 2960, 2927, 2863, 1706, 1671, 1633, 1611, 1531, 1485, 1433, 1385, 1357, 1296, 1223, 1165, 953, 810, 761, 665 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.77 (3H, t, *J* 6.9 Hz, CH_3), 1.10–1.29 (4H, m), 1.72–1.82 (2H, m), 3.93 (2H, s, CH_2Br), 7.09–7.16 (2H, m), 7.62 (1H, ddd, *J* 7.8, 7.8, 1.5 Hz, H-6), 7.76 (1H, dd, *J* 7.8, 1.3 Hz, H-5), 9.24 (1H, br s, NH), 10.92 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 13.5, 21.9, 24.4, 27.8, 35.9, 67.3, 116.3, 118.7, 122.4, 126.8, 136.0, 141.5, 165.7, 170.2, 192.6. Anal. Calcd for $C_{15}H_{17}BrN_2O_3$: C, 51.01; H, 4.85; N, 7.93. Found: C, 50.85; H, 4.79; N, 7.72.

*3.5.2. 2-Bromo-N-butyl-N-(3-butyl-2,4-dioxo-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**7b**)*

White solid; mp 174–176 °C (benzene); IR 3279, 3201, 2958, 2931, 2871, 1710, 1692, 1676, 1662, 1641, 1611, 1599, 1486, 1438, 1361, 1317, 1265, 1251, 1231, 1197, 1096, 928, 882, 764, 690, 666, 640, 618 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.73 (3H, t, *J* 7.1 Hz, CH_3), 0.95 (3H, t, *J* 7.3 Hz, CH_3), 0.92–1.12 (1H, m), 1.13–1.27 (3H, m), 1.30–1.42 (2H, m), 1.71–2.02 (4H, m), 3.56 (2H, t, *J* 8.2 Hz), 4.21 (2H, s, CH_2Br), 7.14–7.17 (2H, m), 7.59 (1H, ddd, *J* 7.7, 7.7, 1.4 Hz, H-7), 7.74 (1H, d, *J* 7.8 Hz, H-5), 10.94 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 13.3, 13.5, 19.4, 22.2, 24.4, 28.1, 33.0, 34.1, 44.5, 71.4, 116.2, 120.0, 122.1, 126.2, 135.5, 141.4, 166.7, 170.7, 193.1. Anal. Calcd for $C_{19}H_{25}BrN_2O_3$: C, 55.75; H, 6.16; N, 6.84. Found: C, 55.62; H, 6.17; N, 6.79.

*3.5.3. N-(3-Benzyl-2,4-dioxo-1,2,3,4-tetrahydroquinolin-3-yl)-2-bromoacetamide (**7c**)*

White solid; mp 120–125 °C (benzene); IR 3254, 3062, 2999, 2928, 2861, 1709, 1667, 1613, 1596, 1486, 1455, 1439, 1385, 1298, 1237, 1212, 1158, 1106, 1031, 960, 942, 765, 748, 701, 684, 666, 636 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 3.11 and 3.18 (2H, 2d, *J* 12.5 Hz, CH_2Ph), 3.95 (2H, s, CH_2Br), 6.76 (1H, d, *J* 8.0 Hz, H-8), 6.91–6.98 (3H, m), 7.02–7.18 (3H, m), 7.38 (1H, ddd, *J* 7.7, 7.7, 1.5 Hz, H-7), 7.60 (1H, dd, *J* 7.8, 1.3 Hz, H-5), 9.51 (1H, br s, NH), 10.78 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 27.8, 43.2, 67.4, 115.8, 119.6, 122.0, 126.0, 127.3, 127.6, 129.8, 131.7, 135.6, 141.2, 165.6, 169.8, 193.2. Anal. Calcd for $C_{18}H_{15}BrN_2O_3$: C, 55.83; H, 3.90; N, 7.23. Found: C, 55.96; H, 3.97; N, 7.17.

*3.5.4. N-(3-Benzyl-2,4-dioxo-1,2,3,4-tetrahydroquinolin-3-yl)-2-bromo-N-butylacetamide (**7d**)*

White solid; mp 175–177 °C (hexane); IR 3236, 3196, 3122, 3087, 3032, 2996, 2931, 2871, 1706, 1671, 1639, 1614, 1599, 1487, 1455, 1440, 1366, 1284, 1256, 1232, 1199, 1156, 1097, 930, 761, 700, 665, 628 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.99 (3H, t, *J* 7.3 Hz, CH_3), 1.35–1.49 (2H, m), 1.82–2.01 (2H, m), 3.26 and 3.33 (2H, 2d, *J* 12.4 Hz, CH_2Ph), 3.72 (2H, br t, *J* 8.2 Hz), 4.24 (2H, s, CH_2Br), 6.62 (1H, d, *J* 8.0 Hz, H-8), 6.88 (1H, dd, *J* 7.5, 7.5 Hz, H-6), 6.88–7.00 (5H, m), 7.27 (1H, ddd, *J* 7.7, 7.7, 1.4 Hz, H-7), 7.55 (1H, dd, *J* 7.8, 1.1 Hz, H-5), 10.67 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 13.6, 19.4, 28.2, 33.3, 41.0, 44.7, 71.5, 115.6, 120.5, 121.5, 125.5, 127.17, 127.24, 130.3, 130.8, 134.8, 140.8, 166.6, 170.2, 193.4. Anal. Calcd for $C_{22}H_{23}BrN_2O_3$: C, 59.60; H, 5.23; N, 6.32. Found: C, 59.32; H, 5.20; N, 6.33.

*3.5.5. 2-Bromo-N-butyl-N-(2,4-dioxo-3-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**7f**)*

White solid; mp 115–122 °C (benzene); IR 3238, 3191, 3163, 3066, 2997, 2960, 2929, 2872, 1715, 1680, 1665, 1642, 1617, 1596, 1488, 1449, 1435, 1354, 1323, 1251, 1228, 1208, 1158, 1122, 1100, 1039, 888, 780, 756, 700, 682, 667, 634, 588, 559, 534, 524, 509, 439 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.53 (3H, t, *J* 7.3 Hz, CH_3), 0.87 (2H, tq, *J* 7.3, 7.3 Hz), 1.35–1.46 (2H, m), 3.12 (2H, t, *J* 8.2 Hz), 4.27 and 4.33 (2H, 2d, *J* 12.3 Hz, CH_2Br), 7.03 (1H, d, *J* 8.5 Hz, H-8), 7.07 (1H, dd, *J* 8.5, 7.6 Hz, H-7), 7.37 (1H, br s, NH), 7.46 (5H, br s, Ph), 7.53 (1H, ddd, *J* 7.8, 7.6, 1.2 Hz, H-7), 7.80 (1H, dd, *J* 7.8, 0.8 Hz, H-5); δ_C (75 MHz, DMSO-d_6) 12.9, 18.9, 28.3, 31.2, 45.8, 77.4, 116.0, 119.3, 122.3, 127.4, 128.2, 129.2, 130.1, 130.3, 135.8, 140.6, 166.9, 168.5, 189.4. Anal. Calcd for $C_{21}H_{21}BrN_2O_3$: C, 58.75; H, 4.93; N, 6.53. Found: C, 59.03; H, 4.82; N, 6.25.

*3.5.6. 2-Bromo-N-(1-methyl-2,4-dioxo-3-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**7g**)*

White solid; mp 216–217 °C (benzene); IR 3329, 3023, 2963, 1712, 1679, 1661, 1602, 1515, 1492, 1474, 1448, 1361, 1301, 1210, 1109, 1037, 896, 780, 766, 731, 697, 687 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 3.53 (3H, s, CH_3), 4.00 and 4.05 (2H, 2d, *J* 11.3 Hz, CH_2Br), 7.20 (1H, dd, *J* 7.5, 7.5 Hz, H-6), 7.28–7.34 (2H, m), 7.34–7.44 (4H, m), 7.72 (1H, ddd, *J* 7.8, 7.8, 1.6 Hz, H-7), 7.83 (1H, dd, *J* 7.7, 1.5 Hz, H-5), 9.71 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 27.8, 30.1, 71.5, 115.9, 119.8, 123.1, 127.2, 127.7, 129.1, 129.5, 132.8, 136.5, 142.0, 166.3, 168.5, 189.3. Anal. Calcd for $C_{18}H_{15}BrN_2O_3$: C, 55.83; H, 3.90; N, 7.23. Found: C, 55.64; H, 4.12; N, 7.04.

*3.5.7. 2-Bromo-N-butyl-N-(1-methyl-2,4-dioxo-3-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**7h**)*

White solid; mp 153–156 °C (benzene/cyclohexane); IR 3072, 3038, 2963, 2932, 2877, 1701, 1667, 1625, 1600, 1492, 1472, 1417, 1348, 1302, 1238, 1215, 1143, 1073, 1026, 993, 887, 768, 751, 705, 663 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.53 (3H, t, *J* 7.3 Hz, CH_3), 0.79–0.96 (2H, m), 1.32–1.50 (2H, m), 3.13 (2H, t, *J* 8.7 Hz), 3.48 (3H, s, NCH_3), 4.28 and 4.33

(2H, 2d, *J* 12.3 Hz, CH_2Br), 7.18 (1H, dd, *J* 7.4, 7.4 Hz, H-6), 7.31 (1H, d, *J* 8.5 Hz, H-8), 7.32–7.39 (2H, m), 7.41–7.49 (3H, m), 7.65 (1H, ddd, *J* 7.8, 7.8, 1.5 Hz, H-7), 7.91 (1H, dd, *J* 7.7, 1.5 Hz, H-5); δ_C (75 MHz, DMSO-d_6) 12.9, 19.0, 26.3, 28.3, 30.1, 31.2, 45.9, 77.5, 115.6, 120.4, 122.8, 127.8, 128.2, 129.3, 130.1, 136.0, 141.6, 166.9, 168.1, 188.5. Anal. Calcd for $C_{22}H_{23}BrN_2O_3$: C, 59.60; H, 5.23; N, 6.32. Found: C, 59.37; H, 5.24; N, 6.17.

3.5.8. 2-Bromo-N-butyl-N-(3-methyl-2,4-dioxo-1-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (*7j*)

White solid; mp 151–156 °C (benzene/cyclohexane); IR 3150–3660, 2952, 2925, 2867, 1709, 1677, 1634, 1602, 1494, 1464, 1367, 1337, 1307, 1258, 1232, 1201, 1162, 1104, 981, 917, 894, 786, 757, 710, 663, 658, 626, 539, 448, 428 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.94 (3H, t, *J* 7.3 Hz, CH_3), 1.37 (2H, m), 1.66 (3H, s, CH_3), 1.65–1.85 (2H, m), 3.61 (2H, t, *J* 8.0 Hz), 4.22 and 4.29 (2H, 2d, *J* 12.2 Hz, CH_2Br), 6.40 (1H, d, *J* 8.4 Hz, H-8), 7.11 (1H, m), 7.21 (1H, dd, *J* 7.5, 7.5 Hz, H-7), 7.42 (1H, m), 7.50–7.67 (4H, m), 7.94 (1H, dd, *J* 6.8, 0.7 Hz, H-5); δ_C (75 MHz, DMSO-d_6) 13.6, 19.4, 19.6, 27.8, 32.9, 44.9, 69.9, 116.5, 118.7, 122.8, 127.7, 128.8, 129.1 (br), 130.1 (br), 135.7, 137.3, 143.3, 166.7, 170.7, 191.7. Anal. Calcd for $C_{22}H_{23}BrN_2O_3$: C, 59.60; H, 5.23; N, 6.32. Found: C, 59.43; H, 5.24; N, 6.31.

3.6. Synthesis of 2-bromo-N-(2,4-dioxo-3-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (*7e*) in THF with triethylamine as a base

To a stirred solution of amine **1e** (1.20 g, 4.76 mmol) in tetrahydrofuran (70 mL), bromoacetyl bromide (1.27 mL, 2.94 g, 14.3 mmol) and then triethylamine (1.46 mL, 1.06 g, 10.4 mmol) were added. The resulting reaction mixture was sealed with a $CaCl_2$ drying tube, stirred at room temperature, and monitored by TLC. Starting **1e** was not consumed until two additional portions of bromoacetyl bromide (1.27 mL, 2.94 g, 14.3 mmol) and triethylamine (0.73 mL, 0.53 g, 5.2 mmol) were added in a 12 h period, and then stirring continued for additional 12 h. The volatile compounds were evaporated on a rotary evaporator at 50 °C. The residue was suspended in chloroform (70 mL) and the suspension was shaken with 2% hydrochloric acid (20 mL). The insoluble material was filtered off, air-dried, and crystallized from ethanol affording **7e** (679 mg, 38% yield). The organic layer of the filtrate was separated, washed with 2% hydrochloric acid (20 mL) and water (2×20 mL), dried over anhydrous sodium sulfate, and evaporated to dryness. The liquid residue was subjected to column chromatography on silica gel using chloroform (to give 5.65 g of 4-bromobutyl bromoacetate as an orange liquid) and subsequently using a mixture of chloroform/ethanol (19:1) as eluting systems to give another crop of impure **7e** (339 mg). Crystallization of the latter from ethanol afforded the second crop of pure **7e** (83 mg, 5%; 43% overall yield, Table 2).

3.6.1. 2-Bromo-N-(2,4-dioxo-3-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (*7e*)

White solid; mp 242–243 °C (ethanol); IR 3520, 3426, 3214, 3184, 3031, 2926, 2856, 1699, 1666, 1613, 1594, 1540, 1485, 1449, 1434, 1371, 1319, 1231, 1210, 1203, 1158, 1115, 1039, 1001, 946, 885, 781, 767, 739, 695, 671, 640, 579, 527, 507, 453, 442 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 4.00 and 4.05 (2H, 2d, *J* 11.2 Hz, CH_2), 7.07–7.16 (2H, m), 7.40 (5H, m, Ph), 7.61 (1H, ddd, *J* 7.7, 7.7, 1.3 Hz, H-6), 7.74 (1H, dd, *J* 7.7, 0.9 Hz, H-5), 9.64 (1H, br s, NH), 11.21 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 27.9, 71.3, 116.4, 118.7, 122.7, 127.2, 127.4, 129.1, 129.4, 132.9, 136.3, 141.1, 166.4, 168.9, 190.4; HRESI-MS calcd for $C_{17}H_{14}{}^{79}BrN_2O_3$ $[M(^{79}Br)+1]^+$ 373.0188, found 373.0197.

Crude 4-bromobutyl bromoacetate obtained as above was purified by chromatography on a silica gel column using benzene. The collected fractions were evaporated and dried under vacuum for 1 h at 100 °C and then in an evacuated desiccator over Sicapent® for 2 days to give pure product as a colorless liquid. IR 2962, 1738, 1436, 1284, 1164, 1111, 1029, 559 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.80–1.90 (2H, m), 1.90–2.02 (2H, m), 3.45 (2H, t, *J* 6.4 Hz), 3.83 (2H, s), 4.22 (2H, t, *J* 6.2 Hz); δ_C (75 MHz, $CDCl_3$) 25.2, 26.6, 28.6, 32.4, 64.8, 164.8. The NMR data are in good agreement with those reported in the literature.[9]

3.7. Synthesis of 2-bromo-N-(2,4-dioxo-3-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (*7e*) in CH_2Cl_2 with triethylamine as a base

To a stirred solution of amine **1e** (0.875 g, 3.47 mmol) in dichloromethane (70 mL), a solution of bromoacetyl bromide (2.22 g, 10.8 mmol) in dichloromethane (5 mL) and subsequently a solution of triethylamine (0.53 g, 5.2 mmol) in dichloromethane (5 mL) were added. The resulting reaction mixture was sealed with a $CaCl_2$ drying tube, stirred at room temperature, and monitored by TLC. After 5 h, additional portions of bromoacetyl bromide (1.43 g, 6.94 mmol) and triethylamine (0.36 g, 3.5 mmol) were added, and then stirring was continued for an additional 14 h. Then 6% aqueous sodium bicarbonate (10 mL) was added and the resulting mixture was stirred for 2 min. The solid material was filtered off, washed with water (20 mL), and crystallized from ethanol to give **7e** (891 mg, 69%). For physical and spectral data, see above.

3.8. Preparation of 3-bromoacetamidoquinoline-2,4(1H,3H)-diones *7f* and *7i* in THF with triethylamine as a base

To an ice-cold stirred solution of the appropriate 3-aminoquinoline-2,4(1*H*,3*H*)-dione **1** (5 mmol) in tetrahydrofuran (15 mL) was added bromoacetyl bromide (1.33 mL, 15 mmol). Then a solution of triethylamine (0.55 g, 5.4 mmol) in tetrahydrofuran (5 mL) was added dropwise for 15 min. The reaction mixture was stirred for 30 min in the ice bath and then for another 30 min at room temperature. The solvents were removed on a rotary evaporator at 80 °C. The residue was dissolved in chloroform (100 mL) and the resulting solution was washed with 2%

hydrochloric acid (3×20 mL) and water (3×20 mL). The chloroform layer was dried over anhydrous sodium sulfate, filtered, and evaporated to dryness. The crude products **7** were purified by crystallization. The yields of analytically pure products are given in Table 2. Physical and spectroscopic data of compounds **7f** and **7i** are listed above and below, respectively.

*3.8.1. 2-Bromo-N-(3-methyl-2,4-dioxo-1-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**7i**)*

White solid; mp 234–236 °C (benzene); IR 3302, 3069, 2982, 2927, 2852, 1728, 1717, 1692, 1682, 1660, 1600, 1582, 1552, 1492, 1464, 1385, 1378, 1343, 1313, 1303, 1272, 1254, 1208, 1182, 1160, 1135, 1108, 1073, 992, 965, 789, 767, 760, 710, 691, 663, 626, 561, 544, 519, 489, 444 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.58 (3H, s, CH_3), 3.95 (2H, s, CH_2), 6.40 (1H, d, *J* 8.3 Hz, H-8), 7.10–7.20 (1H, br s), 7.22 (1H, ddd, *J* 8.3, 6.7, 0.6 Hz, H-7), 7.35–7.48 (1H, br s), 7.50–7.65 (4H, m), 7.94 (1H, dd, *J* 7.8, 1.6 Hz, H-5), 9.55 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 22.7, 28.1, 64.9, 117.0, 119.0, 123.4, 128.1, 129.3, 129.5 (br), 130.6 (br), 136.5, 137.7, 143.9, 166.3, 170.9, 192.6. Anal. Calcd for $C_{18}H_{15}BrN_2O_3$: C, 55.83; H, 3.90; N, 7.23. Found: C, 56.13; H, 4.10; N, 7.24.

*3.9. General procedure for the synthesis of triphenylphosphonium bromides **8a**,**c**,**f**,**g***

A suspension of the appropriate bromoacetamide **7** (1.3 mmol) and triphenylphosphine (375 mg, 1.43 mmol) in benzene (10 mL) was heated at reflux for the time given in Table 3. After cooling, the precipitated phosphonium bromide **8** was suction filtered and washed with benzene. Products **8a**,**c**,**f** were purified by crystallization from the solvents given below and **8g** was used for further transformations without purification. In the cases of **8c** and **8g**, the mother liquors after filtration were combined, evaporated to dryness, and the residues were column chromatographed on silica gel using benzene and then using successive mixtures of benzene/ethyl acetate (in ratios from 99:1 to 8:2) as eluents to give 3-acetamidoquinoline-2,4(1*H*,3*H*)-diones **9c** and **9g**. The yields of the products are given in Table 3 and the spectral and analytical data are given below.

*3.9.1. (2-(3-Butyl-2,4-dioxo-1,2,3,4-tetrahydroquinolin-3-ylamino)-2-oxoethyl)triphenylphosphonium bromide (**8a**)*

White solid; mp 252–262 °C (ethyl acetate); IR 3180, 3127, 3051, 3022, 2958, 2870, 1712, 1673, 1612, 1540, 1484, 1437, 1360, 1244, 1111, 1043, 997, 946, 815, 749, 720, 688 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.78 (3H, t, *J* 7.0 Hz, CH_3), 1.13–1.22 (4H, m, $CH_3CH_2CH_2$), 1.70–1.81 (2H, m, $CH_3CH_2CH_2CH_2$), 5.14 (2H, d, $^2J_{PH}$ 15.1 Hz, CH_2P), 7.09 (1H, d, *J* 7.7 Hz, H-8), 7.10 (1H, dd, *J* 7.7, 7.7 Hz, H-6), 7.60 (1H, ddd, *J* 7.7, 7.7, 1.6 Hz, H-7), 7.69–7.77 (13H, m, H-5, 3×(H-2″, H-3″, H-5″, H-6″)), 7.83–7.92 (3H, m, 3×H-4″), 9.56 (1H, br s, NHCO), 10.97 (1H, br s, H-1); δ_C (75 MHz, DMSO-d_6) 13.5 (CH_3), 21.8 (CH_3CH_2), 24.5 ($CH_3CH_2CH_2$), 29.6 (d, $^1J_{CP}$ 58.2 Hz, CH_2P), 35.7 ($CH_3CH_2CH_2CH_2$), 68.2 (C-3), 116.3 (C-8), 118.36 (C-4a), 118.43 (d, $^1J_{CP}$ 88.8 Hz, C-1″), 122.5 (C-6), 126.9 (C-5), 129.9 (d, J_{CP} 13.0 Hz, C-2″, C-6″ or C-3″, C-5″), 133.6 (d, J_{CP} 10.7 Hz, C-3″, C-5″ or C-2″, C-6″), 134.8 (d, $^4J_{CP}$ 2.7 Hz, C-4″), 136.2 (C-7), 141.3 (C-8a), 162.8 (d, $^2J_{CP}$ 5.0 Hz, CONH), 169.6 (C-2), 191.9 (C-4); δ_P (121 MHz, DMSO-d_6) 25.0. Anal. Calcd for $C_{33}H_{32}BrN_2O_3P$: C, 64.40; H, 5.24; N, 4.55. Found: C, 64.14; H, 5.19; N, 4.25.

*3.9.2. (2-(3-Benzyl-2,4-dioxo-1,2,3,4-tetrahydroquinolin-3-ylamino)-2-oxoethyl)triphenylphosphonium bromide (**8c**)*

White solid; mp 251–254 °C (ethanol/ethyl acetate); IR 3181, 3083, 2990, 2868, 1713, 1678, 1665, 1611, 1596, 1585, 1524, 1484, 1438, 1372, 1356, 1335, 1323, 1246, 1111, 1029, 997, 945, 768, 748, 719, 687 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 3.17 (2H, 2d, *J* 12.7 Hz, CH_2Ph), 5.15 (2H, d, $^2J_{PH}$ 15.0 Hz, CH_2P), 6.73 (1H, d, *J* 8.0 Hz, H-8), 6.92–7.09 (6H, m, H-6, H-2′, H-3′, H-4′, H-5′, H-6′), 7.37 (1H, ddd, *J* 7.7, 7.7, 1.4 Hz, H-7), 7.57 (1H, dd, *J* 7.7, 1.0 Hz, H-5), 7.65–7.78 (12H, m, 3×(H-2″, H-3″, H-5″, H-6″)), 7.82–7.92 (3H, m, 3×H-4″), 9.79 (1H, br s, CONH), 10.83 (1H, br s, H-1); δ_C (75 MHz, DMSO-d_6) 29.9 (d, $^1J_{CP}$ 59.0 Hz, CH_2P), 43.2, 68.1 (C-3), 115.9, 118.4 (d, $^1J_{CP}$ 88.9 Hz, C-1″), 119.3, 122.2, 126.2, 127.3, 127.6, 129.8, 129.9 (d, J_{CP} 13.0 Hz, C-2″, C-6″ or C-3″, C-5″), 131.4, 133.6 (d, J_{CP} 10.8 Hz, C-3″, C-5″ or C-2″, C-6″), 134.8 (d, $^4J_{CP}$ 2.7 Hz, C-4″), 135.9 (C-7), 141.0 (C-8a), 162.7 (d, $^2J_{CP}$ 4.9 Hz, CONH), 169.3, 192.5; δ_P (121 MHz, DMSO-d_6) 25.0. Anal. Calcd for $C_{36}H_{30}BrN_2O_3P$: C, 66.57; H, 4.66; N, 4.31. Found: C, 66.59; H, 4.73; N, 4.22.

*3.9.3. (2-(Butyl(2,4-dioxo-3-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)amino)-2-oxoethyl)triphenylphosphonium bromide (**8f**)*

Yellowish solid; mp 177–183 °C (ethanol/ethyl acetate); IR 3270–3680, 3058, 2962, 2908, 2870, 2856, 1713, 1680, 1632, 1613, 1596, 1485, 1438, 1428, 1366, 1346, 1321, 1250, 1225, 1198, 1160, 1109, 1039, 1029, 888, 865, 852, 794, 766, 749, 720, 701, 687, 660, 588, 544, 511, 498, 480, 440 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.55 (3H, t, *J* 7.4 Hz, CH_3), 0.88 (2H, m), 1.55 (2H, m), 3.27 (2H, m), 5.62 (2H, d, $^2J_{PH}$ 14.2 Hz, CH_2P), 6.93 (1H, d, *J* 8.1 Hz), 7.03 (1H, dd, *J* 7.4, 7.4 Hz), 7.37–7.90 (22H, m), 11.18 (1H, br s, H-1); δ_C (75 MHz, DMSO-d_6) 12.8 (CH_3), 19.0 (CH_3CH_2), 30.3 (d, $^1J_{CP}$ 65.7 Hz, CH_2P), 30.5 ($CH_3CH_2CH_2$), 46.3 ($CH_3CH_2CH_2CH_2$), 78.0 (C-3), 116.1, 119.2, 119.3 (d, $^1J_{CP}$ 89.8 Hz, C-1″), 122.5, 127.4, 128.0, 129.6 (d, J_{CP} 12.9 Hz, C-2″, C-6″ or C-3″, C-5″), 133.6 (d, J_{CP} 10.5 Hz, C-3″, C-5″ or C-2″, C-6″), 134.3 (d, $^4J_{CP}$ 2.7 Hz, C-4″), 135.9 (C-7), 140.2 (C-8a), 165.4 (d, $^2J_{CP}$ 4.1 Hz, CONH), 167.9 (C-2), 189.2 (C-4); δ_P (121 MHz, DMSO-d_6) 25.2; HRESI-MS calcd for $C_{39}H_{36}N_2O_3P$ $[M-Br]^+$ 611.2464, found 611.2460.

*3.9.4. (2-(1-Methyl-2,4-dioxo-3-phenyl-1,2,3,4-tetrahydroquinolin-3-ylamino)-2-oxoethyl)triphenylphosphonium bromide (**8g**)*

White solid; mp 229–233 °C; IR 3171, 3054, 2990, 2842, 1713, 1676, 1601, 1513, 1490, 1472, 1437, 1354, 1298, 1111, 997, 859, 781, 772, 750, 721, 691, 641 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 3.49 (3H, s, CH_3), 5.11 (2H, m, CH_2P), 7.18

(1H, dd, *J* 7.3, 7.3 Hz), 7.22–7.96 (23H, m), 9.83 (1H, s, NH); δ_C (75 MHz, DMSO-d_6) 29.6 (d, $^1J_{CP}$ 57.2 Hz, CH_2P), 30.2 (CH_3), 72.0 (C-3), 116.0, 118.3 (d, $^1J_{CP}$ 88.6 Hz, C-1″), 119.5, 123.3, 127.0, 127.7, 129.3, 129.7, 130.0 (d, J_{CP} 12.9 Hz, C-2″, C-6″ or C-3″, C-5″), 132.5, 133.7 (d, J_{CP} 10.7 Hz, C-3″, C-5″ or C-2″, C-6″), 134.8 (d, $^4J_{CP}$ 2.8 Hz, C-4″), 136.7 (C-7), 141.8 (C-8a), 163.1 (d, $^2J_{CP}$ 5.2 Hz, CONH), 167.9, 188.9; δ_P (121 MHz, DMSO-d_6) 25.1; FABMS *m/z* (%) 569 ([M−Br]$^+$, 100), 303 (30); HRESI-MS calcd for $C_{36}H_{30}N_2O_3P$ [M−Br]$^+$ 569.1994, found 569.2001.

3.9.5. (2-(2,4-Dioxo-3-phenyl-1,2,3,4-tetrahydroquinolin-3-ylamino)-2-oxoethyl)triphenylphosphonium bromide (8e)

A mixture of bromoacetamide **7e** (716 mg, 1.92 mmol) and triphenylphosphine (577 mg, 2.20 mmol) in 1,4-dioxane (16 mL) was refluxed (KOH—seal) for 13 h. The reaction mixture was allowed to cool to room temperature and the solid material was filtered. The filter cake was washed with 1,4-dioxane (1.5 mL) and air-dried at room temperature to a constant mass yielding **8e** (792 mg, 62%).

Compound ***8e***: white solid; mp 256–263 °C; IR 3181, 3145, 3124, 3079, 3058, 3012, 2977, 2965, 2928, 2912, 2900, 2872, 2859, 2768, 1716, 1678, 1673, 1611, 1585, 1529, 1485, 1439, 1393, 1351, 1328, 1248, 1229, 1160, 1112, 997, 943, 867, 749, 721, 689, 571, 515, 497 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 5.11 (2H, m, CH_2P), 7.05–7.11 (2H, m), 7.32–7.43 (5H, m), 7.59 (1H, ddd, *J* 8.0, 8.0, 1.5 Hz, H-7), 7.68 (1H, dd, *J* 8.0, 1.5 Hz, H-5), 7.72–7.82 (12H, m, 3×(H-2″, H-3″, H-5″, H-6″)), 7.85–7.93 (3H, m, 3×H-4″), 9.78 (1H, br s, NHCO), 11.27 (1H, br s, H-1); δ_C (75 MHz, DMSO-d_6) 29.6 (d, $^1J_{CP}$ 57.1 Hz, CH_2P), 71.8 (C-3), 116.4, 118.3 (d, $^1J_{CP}$ 88.7 Hz, C-1″), 118.4, 122.9, 127.0, 127.4, 129.2, 129.7, 129.9 (d, J_{CP} 13.0 Hz, C-2″, C-6″ or C-3″, C-5″), 132.5, 133.7 (d, J_{CP} 10.7 Hz, C-3″, C-5″ or C-2″, C-6″), 134.8 (d, $^4J_{CP}$ 2.8 Hz, C-4″), 136.5 (C-7), 140.8 (C-8a), 163.1 (d, $^2J_{CP}$ 5.1 Hz, CONH), 168.3 (C-2), 189.9 (C-4); δ_P (121 MHz, DMSO-d_6) 25.0; HRESI-MS calcd for $C_{35}H_{28}N_2O_3P$ [M−Br]$^+$ 555.1838, found 555.1820.

3.9.6. (2-(3-Methyl-2,4-dioxo-1-phenyl-1,2,3,4-tetrahydroquinolin-3-ylamino)-2-oxoethyl)triphenylphosphonium bromide (8i)

A mixture of bromoacetamide **7i** (548 mg, 1.42 mmol), triphenylphoshine (427 mg, 1.63 mmol), and benzene (7 mL) was heated at reflux (KOH—seal) for 8 h. Two layers were formed after cooling. The upper less-viscous layer was removed and the bottom oily layer was extracted with benzene (2×4 mL). Repeated crystallization of the refined oily layer from ethanol/ethyl acetate mixture of solvents afforded **8i** (243 mg, 26%). Collected mother liquors after crystallizations were evaporated in vacuo and subjected to column chromatography on silica gel using chloroform and then successive mixtures of chloroform/ethanol in ratios 99:1 and 98:2 to give crude compounds **9i** and **3i** in sequence. Crystallization of these two crude products gave pure compounds **9i** (125 mg, 29%) and **3i** (11 mg, 2.5%).

Compound ***8i***: white solid; mp 179–186 °C (ethanol/ethyl acetate); IR 3100–3680 (br), 3169, 3010, 2994, 2870, 1709, 1674, 1650, 1599, 1491, 1464, 1439, 1375, 1335, 1262, 1141, 1111, 997, 862, 755, 745, 732, 707, 690, 514, 503 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.62 (3H, s, CH_3), 5.11 (2H, m, CH_2P), 6.36 (1H, d, *J* 8.4 Hz, H-8), 6.92 (1H, br s), 7.20 (1H, dd, *J* 7.5, 7.5 Hz, H-6), 7.43 (1H, br s), 7.50–7.92 (20H, m), 9.89 (1H, br s, H-1); δ_C (75 MHz, DMSO-d_6) 22.5 (CH_3), 29.8 (d, $^1J_{CP}$ 59.8 Hz, CH_2P), 65.0 (C-3), 116.6 (C-8), 118.4 (C-4a), 118.5 (d, $^1J_{CP}$ 88.8 Hz, C-1″), 123.2 (C-6), 127.8 (C-5), 128.8 (br), 129.0, 129.9 (d, J_{CP} 12.9 Hz, C-2″, C-6″ or C-3″, C-5″), 130.2, 133.7 (d, J_{CP} 10.6 Hz, C-3″, C-5″ or C-2″, C-6″), 134.8 (d, $^4J_{CP}$ 2.7 Hz, C-4″), 136.3 (C-7), 137.0, 143.3, 163.1 (d, $^2J_{CP}$ 5.0 Hz, CONH), 170.2 (C-2), 191.6 (C-4); δ_P (121 MHz, DMSO-d_6) 25.1; HRESI-MS calcd for $C_{36}H_{30}N_2O_3P$ [M−Br]$^+$ 569.1994, found 569.2017.

3.10. Transformation of 3-bromoacetamidoquinoline-2,4(1H,3H)diones (7b,d,h,j; R^3=n-butyl) to pyrrolo[2,3-c]-quinoline-2,4(3aH,5H)-diones 3b,d,h and 3-acetamidoquinolinediones 9b,d,h,j

A solution of the appropriate 3-bromoacetamidoquinoline-2,4(1*H*,3*H*)-dione **7** (4 mmol) and triphenylphosphine (1.154 g, 4.4 mmol) in benzene (30 mL) was heated at reflux for 4 h. The reaction mixture was evaporated to dryness, redissolved in chloroform (30 mL), and extensively shaken with aqueous sodium hydroxide (0.5 M, 10 mL) for 5 min. The layers were separated and the chloroform layer was washed with water (2×10 mL). Organic layer was dried over anhydrous sodium sulfate, filtered, and evaporated to dryness. The residue was subjected to column chromatography on silica gel using benzene and then using successive mixtures of benzene/ethyl acetate (in ratios from 99:1 to 8:2) as eluents to give pyrrolo[2,3-*c*]quinoline-2,4(3a*H*,5*H*)-diones **3b**,**d**,**h** and 3-acetamidoquinolinediones **9b**,**d**,**h**. Using this procedure, compound **7j** only afforded the corresponding 3-acetamidoquinolinediones **9j**. The yields of the products are given in Table 4.

3.11. General procedure for the preparation of pyrrolo-[2,3-c]quinoline-2,4-(3aH,5H)-diones 3a,c,e,g from phosphonium salts 8a,c,e,g

A solution of the corresponding phosphonium salt **8** (0.18 mmol) in chloroform (10 mL) was extensively shaken with aqueous sodium hydroxide (0.5 M, 8 mL) for 5 min. The precipitated product **3** was suction filtered, washed with chloroform, and crystallized from the solvent given below.

In the case of **3f**, which after the above procedure remained dissolved in chloroform, the organic layer was separated, dried over Na_2SO_4, and evaporated to dryness. The oily residue was triturated consecutively with hexane, cyclohexane, and diethyl ether affording crystalline **3f**.

The yields of the products are given in Table 3. For the physical and spectroscopic data see above.

3.12. Independent synthesis of 3-acetamidoquinoline-2,4(1H,3H)diones **9** from 3-aminoquinoline-2,4(1H,3H)-diones **1**

3.12.1. General procedure for the preparation of **9a–d,g–i**

To a solution of 3-aminoquinoline-2,4(1*H*,3*H*)-dione **1** (0.31 mmol) in pyridine (3 mL), acetic anhydride (98%, 0.5 mL, 5 mmol) was added. The reaction mixture was stirred at room temperature for 6 h (**9a–c**) or heated at 60 °C for 1 h (**9d,g–i**), the volatile compounds were evaporated to dryness in vacuo, and the residue was crystallized from the solvents indicated below. The yields are listed in Table 5.

*3.12.1.1. N-(3-Butyl-2,4-dioxo-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**9a**).* White solid; mp 242–245 °C (benzene); IR 3354, 3163, 3060, 2927, 1705, 1667, 1644, 1611, 1541, 1485, 1438, 1368, 1357, 1296, 1254, 1163, 1037, 949, 760, 666 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.76 (3H, t, *J* 6.7 Hz, CH_3), 1.07–1.28 (4H, m), 1.74 (2H, t, *J* 7.7 Hz), 1.85 (3H, s, $COCH_3$), 7.10 (1H, dd, *J* 7.2, 7.2 Hz, H-7), 7.11 (1H, d, *J* 7.7 Hz, H-8), 7.59 (1H, dd, *J* 7.5, 7.5 Hz, H-6), 7.75 (1H, d, *J* 7.4 Hz, H-5), 8.82 (1H, br s, NH), 10.86 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 13.5, 21.2, 22.0, 24.4, 35.9, 67.0, 116.2, 119.0, 122.2, 126.7, 135.8, 141.6, 169.1, 171.0, 193.3. Anal. Calcd for $C_{15}H_{18}N_2O_3$: C 65.68; H, 6.61; N, 10.21. Found: C, 65.60; H, 6.69; N, 9.99.

*3.12.1.2. N-Butyl-N-(3-butyl-2,4-dioxo-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**9b**).* White solid; mp 114–116 °C (benzene/cyclohexane); IR 3195, 3070, 2959, 2929, 2867, 1697, 1666, 1632, 1614, 1487, 1431, 1414, 1369, 1362, 1255, 1208, 1157, 1029, 908, 807, 757, 692, 666 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.72 (3H, t, *J* 7.0 Hz), 0.91–1.05 (4H, m), 1.12–1.27 (3H, m), 1.30–1.42 (2H, m), 1.68–1.98 (4H, m), 2.01 (3H, s, $COCH_3$), 3.50 (2H, t, *J* 8.1 Hz), 7.07 (1H, dd, *J* 7.5, 7.5 Hz, H-6), 7.10 (1H, d, *J* 8.1 Hz, H-8), 7.56 (1H, ddd, *J* 7.7, 7.7, 1.5 Hz, H-7), 7.73 (1H, dd, *J* 7.8, 1.0 Hz, H-5), 10.87 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 13.4, 13.6, 19.5, 21.1, 22.3, 24.4, 33.0, 34.2, 44.6, 70.7, 116.2, 120.2, 121.9, 126.1, 135.3, 141.4, 170.5, 171.4, 193.6; HRESI-MS calcd for $C_{19}H_{27}N_2O_3$ $[M+1]^+$ 331.2022, found 331.2011.

*3.12.1.3. N-(3-Benzyl-2,4-dioxo-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**9c**).* White solid; mp 232–236 °C (methanol); IR 3379, 3227, 3180, 3060, 2930, 1707, 1660, 1640, 1611, 1509, 1485, 1434, 1380, 1366, 1298, 1282, 1235, 1163, 1110, 1037, 940, 825, 774, 738, 698, 666 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.86 (3H, s, $COCH_3$), 3.07 and 3.14 (2H, 2d, *J* 12.5 Hz, CH_2), 6.74 (1H, d, *J* 8.0 Hz, H-8), 6.89–6.98 (3H, m), 6.98–7.06 (3H, m), 7.35 (1H, ddd, *J* 7.6, 7.6, 1.5 Hz, H-7), 7.59 (1H, dd, *J* 7.8, 1.3 Hz, H-5), 9.09 (1H, br s, NH), 10.69 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 21.2, 43.2, 67.2, 115.7, 119.7, 121.8, 125.9, 127.1, 127.5, 129.7, 132.0, 135.4, 141.2, 169.0, 170.5, 193.9. Anal. Calcd for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.09. Found: C, 69.68; H, 5.22; N, 8.94.

*3.12.1.4. N-(3-Benzyl-2,4-dioxo-1,2,3,4-tetrahydroquinolin-3-yl)-N-butylacetamide (**9d**).* White solid; mp 270–273 °C (methanol); IR 3224, 3158, 2996, 2929, 1703, 1670, 1613, 1599, 1486, 1431, 1370, 1285, 1257, 1206, 1154, 1077, 1011, 929, 822, 763, 699, 666 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.99 (3H, t, *J* 7.3 Hz, CH_3), 1.34–1.48 (2H, m), 1.77–1.82 (2H, m), 2.04 (3H, s, $COCH_3$), 3.21 and 3.28 (2H, 2d, *J* 11.6 Hz, CH_2), 3.60–3.70 (2H, m), 6.60 (1H, d, *J* 8.0 Hz, H-8), 6.85 (1H, ddd, *J* 7.5, 7.5, 0.8 Hz, H-6), 6.88–6.99 (5H, m), 7.24 (1H, ddd, *J* 7.6, 7.6, 1.4 Hz, H-7), 7.53 (1H, dd, *J* 7.8, 1.3 Hz, H-5), 10.58 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 13.7, 19.5, 21.1, 33.2, 41.1, 44.8, 70.9, 115.5, 120.6, 121.3, 125.4, 127.1, 127.2, 130.2, 131.1, 134.5, 140.7, 170.4, 170.9, 193.8. Anal. Calcd for $C_{22}H_{24}N_2O_3$: C, 72.51; H, 6.64; N, 7.69. Found: C, 72.54; H, 6.69; N, 7.49.

*3.12.1.5. N-Butyl-N-(2,4-dioxo-3-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**9f**).* White solid; mp 222–224 °C (ethanol/ethyl acetate); IR 3229, 3165, 3139, 3121, 3100, 3065, 2995, 2964, 2927, 2859, 1713, 1676, 1613, 1604, 1508, 1496, 1486, 1464, 1450, 1433, 1347, 1322, 1307, 1255, 1241, 1226, 1211, 1176, 1156, 1124, 1077, 1036, 942, 880, 771, 758, 750, 699, 686, 669, 622, 590, 539, 525, 510, 438 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.57 (3H, t, *J* 7.3 Hz, CH_3), 0.80–0.97 (2H, m), 1.25–1.45 (2H, m), 2.11 (3H, s, CH_3), 3.00–3.12 (2H, m), 6.98–7.10 (2H, m), 7.38–7.55 (6H, m), 7.78 (1H, d, *J* 7.3 Hz), 11.1 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 13.9, 20.0, 22.3, 32.2, 46.9, 77.9, 116.9, 120.3, 123.1, 128.3, 129.9, 130.1, 130.8, 131.2, 136.5, 141.6, 170.1, 171.7, 190.9; HRESI-MS calcd for $C_{21}H_{23}N_2O_3$ $[M+1]^+$ 351.1709, found 351.1720.

*3.12.1.6. N-(1-Methyl-2,4-dioxo-3-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**9g**).* White solid; mp 225–229 °C (benzene); IR 3329, 3272, 3035, 1706, 1657, 1645, 1474, 1449, 1361, 1291, 1252, 1126, 1039, 996, 894, 769, 760, 704, 675 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.92 (3H, s, $COCH_3$), 3.51 (3H, s, NCH_3), 7.18 (1H, dd, *J* 7.4, 7.4 Hz, H-6), 7.27–7.38 (5H, m), 7.40 (1H, d, *J* 8.5 Hz, H-8), 7.71 (1H, ddd, *J* 7.8, 7.8, 1.3 Hz, H-7), 7.81 (1H, dd, *J* 7.6, 1.1 Hz, H-5), 9.31 (1H, s, NH); δ_C (75 MHz, DMSO-d_6) 21.2, 30.0, 71.3, 115.8, 119.9, 122.9, 127.2, 127.6, 128.9, 129.2, 133.2, 136.2, 142.1, 169.3, 169.9, 189.9. Anal. Calcd for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.09. Found: C, 69.84; H, 5.11; N, 9.03.

*3.12.1.7. N-Butyl-N-(1-methyl-2,4-dioxo-3-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**9h**).* White solid; mp 167–169 °C (cyclohexane); IR 3070, 2964, 2932, 1701, 1667, 1625, 1600, 1493, 1472, 1417, 1404, 1348, 1302, 1238, 1215, 1144, 1073, 1026, 993, 930, 887, 768, 751, 706, 663 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.56 (3H, t, *J* 7.3 Hz, CH_3), 0.83–0.97 (2H, m), 1.28–1.48 (2H, m), 2.10 (3H, s, $COCH_3$), 3.01–3.12 (2H, m), 3.46 (3H, s, NCH_3), 7.16 (1H, ddd, *J* 7.5, 7.5, 0.6 Hz, H-6), 7.29 (1H, d, *J* 8.3 Hz, H-8), 7.32–7.48 (5H, m), 7.63 (1H, ddd, *J* 7.8, 7.8, 1.2 Hz, H-7),

7.89 (1H, dd, *J* 7.7, 1.6 Hz, H-5); δ_C (75 MHz, DMSO-d_6) 13.0, 19.0, 21.4, 30.0, 31.2, 46.0, 77.1, 115.5, 120.5, 122.7, 127.7, 129.0, 129.2, 129.9, 130.0, 135.8, 141.6, 168.7, 170.8, 189.0. Anal. Calcd for $C_{22}H_{24}N_2O_3$: C, 72.50; H, 6.64; N, 7.69. Found: C, 72.40; H, 6.61; N, 7.79.

*3.12.1.8. N-(3-Methyl-2,4-dioxo-1-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**9i**).* White solid; mp 245–247 °C (benzene); IR 3297, 3065, 2984, 1721, 1686, 1651, 1601, 1543, 1492, 1463, 1377, 1341, 1301, 1253, 1209, 1181, 1159, 1138, 1109, 1072, 1024, 989, 853, 788, 760, 711, 691, 664, 614, 586, 523, 499, 448 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.53 (3H, s, CH_3), 1.87 (3H, s, $COCH_3$), 6.37 (1H, d, *J* 8.3 Hz, H-8), 7.03–7.23 (1H, br s), 7.20 (1H, dd, *J* 8.3, 6.4 Hz, H-7), 7.34–7.48 (1H, br s), 7.50–7.68 (4H, m), 7.93 (1H, dd, *J* 7.8, 1.5 Hz, H-5), 9.13 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 21.6, 22.5, 64.5, 116.9, 119.1, 123.3, 128.1, 128.7, 129.2 (br), 130.6 (br), 136.3, 137.8, 144.0, 169.7, 171.7, 193.2. Anal. Calcd for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.09. Found: C, 70.27; H, 5.52; N, 9.07.

*3.12.2. Preparation of N-(2,4-dioxo-3-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**9e**)*

A suspension of **1e** (505 mg, 2.00 mmol) in toluene (70 mL) and 98% acetic anhydride (0.6 mL, 6 mmol) was stirred and heated at reflux for 4 h and then stirring was continued at room temperature for an additional 4 h. The solids were filtered off and dried to give pure **9e** (512 mg, 87%), which for analyses was re-crystallized from propan-2-ol (68% overall yield, see Table 5).

*Compound **9e**:* white solid; mp 286–289 °C (propan-2-ol); IR 2820–3670, 3384, 3363, 3184, 3168, 3135, 3094, 3060, 3040, 2994, 2925, 2864, 1709, 1671, 1644, 1613, 1594, 1516, 1486, 1450, 1438, 1429, 1358, 1325, 1290, 1254, 1231, 1183, 1165, 1116, 1108, 1040, 1003, 943, 876, 818, 785, 767, 735, 696, 667, 574, 526, 507, 460, 438 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.93 (3H, s, CH_3), 7.05–7.13 (2H, m), 7.34–7.41 (5H, m), 7.58 (1H, ddd, *J* 7.6, 7.6, 1.2 Hz, H-7), 7.72 (1H, dd, *J* 7.7, 1.2 Hz, H-5), 9.24 (1H, br s, NH), 11.13 (1H, br s, NH); δ_C (75 MHz, DMSO-d_6) 21.3, 71.1, 116.3, 118.7, 122.5, 127.2, 127.3, 128.9, 129.1, 133.2, 136.0, 141.1, 169.6, 169.9, 191.0. Anal. Calcd for $C_{17}H_{14}N_2O_3$: C, 69.38; H, 4.80; N, 9.52. Found: C, 69.16; H, 4.88; N, 9.57.

*3.12.3. N-Butyl-N-(2,4-dioxo-3-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**9f**)*

Pyridine (0.95 mL, 12 mmol) and acetic anhydride (98%, 1.52 mL, 15.8 mmol) were added to a solution of **1f** (1.213 g, 3.93 mmol) in toluene (80 mL). The mixture was stirred at 60 °C for 1 h, followed by the addition of a second aliquot of pyridine (0.95 mL, 12 mmol). The homogeneous mixture was stirred at 65–75 °C for 4 h. Then stirring was continued without heating overnight. The resulting precipitate was filtered off to give crude **9f** (1.096 g). The filtrate was concentrated in vacuo to approximately 10 mL, from which the second crop of crude **9f** (310 mg) was filtered off. Crystallization of the combined crops (both being pure according to TLC analysis) afforded **9f** (929 mg, 67%).

*3.12.4. Preparation of N-(3-methyl-2,4-dioxo-1-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**9i**) in toluene*

To a stirred solution of **1i** (370 mg, 1.39 mmol) in toluene (35 mL) at 27 °C, acetic anhydride (98%, 0.19 mL, 2.0 mmol) was added and then stirring was continued for 1 h. The reaction mixture was left at 10 °C overnight and the resulting precipitate was filtered off to give crude **9i** (329.5 mg). The filtrate was concentrated in vacuo to approximately 5 mL and the second crop of crude **9i** (62.7 mg) was obtained by filtration. Crystallization of the combined crops (both being pure according to TLC analysis) afforded **9i** (301 mg, 70%).

*3.12.5. N-Butyl-N-(3-methyl-2,4-dioxo-1-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**9j**)*

A solution of **1j** (484 mg, 1.5 mmol) and acetic anhydride (98%, 0.22 mL, 2.3 mmol) in toluene (35 mL) was stirred at room temperature for 3 days. The second portion of acetic anhydride (2.10 mL, 22 mmol) was added. The next day, pyridine (0.32 mL, 4.0 mmol) was added in two equal portions at 9 h interval. After stirring the reaction mixture overnight, the solvent was evaporated in vacuo to give an oily residue from which a solid precipitated upon workup with hexane (10 °C). Filtration and crystallization afforded **9j** (339 mg, 62%).

*3.12.6. N-Butyl-N-(3-methyl-2,4-dioxo-1-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)acetamide (**9j**)*

White solid; mp 144–148 °C (cyclohexane); IR 3061, 3036, 3008, 2986, 2967, 2952, 2933, 2871, 1703, 1671, 1631, 1601, 1496, 1483, 1464, 1423, 1379, 1370, 1359, 1342, 1308, 1266, 1242, 1217, 1199, 1163, 1199, 1163, 1103, 1018, 1001, 984, 894, 758, 749, 709, 692, 661, 608, 541, 446 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 0.95 (3H, t, *J* 7.3 Hz, CH_3CH_2), 1.31–1.41 (2H, m, CH_3CH_2), 1.61 (3H, s, CH_3–(C-3)), 1.64–1.74 (2H, m, $CH_3CH_2CH_2$), 2.06 (3H, s, $COCH_3$), 3.55 (2H, br t, *J* 8.1 Hz, $CH_3CH_2CH_2CH_2$), 6.38 (1H, d, *J* 8.3 Hz, H-8), 7.11 (1H, br d, *J* 6.7 Hz, H-2′ (H-6′)), 7.19 (1H, dd, *J* 7.5, 7.5 Hz, H-6), 7.40 (1H, br d, *J* 6.5 Hz, H-6′ (H-2′)), 7.52 (2H, m, H-7, H-4′), 7.56–7.66 (2H, m, H-3′, H-5′), 7.93 (1H, dd, *J* 7.7, 1.4 Hz, H-5); δ_C (75 MHz, DMSO-d_6) 13.7 (CH_3CH_2), 19.4 and 19.5 (CH_3CH_2 and CH_3-(C-3)), 20.9 (CH_3CO), 32.8 ($CH_3CH_2CH_2$), 44.9 ($CH_3CH_2CH_2CH_2$), 69.1 (C-3), 116.3 (C-8), 118.8 (C-4a), 122.6 (C-6), 127.6 (C-5), 128.7 (C-4′), 129.0 (br, C-2′, C-6′), 130.0 (br, C-3′, C-5′), 135.4 (C-7), 137.5 (C-1′), 143.2 (C-8a), 170.5 ($COCH_3$), 171.3 (C-2), 192.2 (C-4); δ_C (75 MHz, DMSO-d_6, 373 K) 13.5, 19.5, 19.8, 20.9, 33.0, 45.2, 69.4, 116.4, 119.3, 122.6, 127.7, 128.6, 129.1, 129.9, 135.2, 137.9, 143.5, 170.6, 171.4, 192.1. Anal. Calcd for $C_{22}H_{24}N_2O_3$: C, 72.51; H, 6.64; N, 7.69. Found: C, 72.30; H, 6.80; N, 7.62.

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References and notes

1. (a) Klásek, A.; Kořistek, K.; Polis, J.; Košmrlj, J. *Heterocycles* **1998**, *48*, 2309–2326; (b) Klásek, A.; Kořistek, K.; Polis, J.; Košmrlj, J. *Tetrahedron* **2000**, *56*, 1551–1560; (c) Klásek, A.; Polis, J.; Mrkvička, V.; Košmrlj, J. *J. Heterocycl. Chem.* **2002**, *39*, 1315–1320; (d) Klásek, A.; Kořistek, K.; Kafka, S.; Košmrlj, J. *Heterocycles* **2003**, *60*, 1811–1820; (e) Klásek, A.; Mrkvička, V.; Pevec, A.; Košmrlj, J. *J. Org. Chem.* **2004**, *69*, 5646–5651; (f) Košmrlj, J.; Kafka, S.; Leban, I.; Grad, M. *Magn. Reson. Chem.* **2007**, *45*, 700–704; (g) Pomeisl, K.; Kvíčala, J.; Paleta, O.; Klásek, A.; Kafka, S.; Kubelka, V.; Havlíček, J.; Čejka, J. *Tetrahedron* **2007**, *63*, 10549–10561; (h) Kafka, S.; Košmrlj, J.; Klásek, A.; Pevec, A. *Tetrahedron Lett.* **2008**, *49*, 90–93.
2. Kafka, S.; Klásek, A.; Polis, J.; Košmrlj, J. *Heterocycles* **2002**, *57*, 1659–1682.
3. (a) Klásek, A.; Lyčka, A.; Holčapek, M.; Hoza, I. *Tetrahedron* **2004**, *60*, 9953–9961; (b) Klásek, A.; Kořistek, K.; Lyčka, A.; Holčapek, M. *Tetrahedron* **2003**, *59*, 5279–5288; (c) Klásek, A.; Lyčka, A.; Holčapek, M.; Hoza, I. *J. Heterocycl. Chem.* **2006**, *43*, 1251–1260.
4. Kafka, S.; Kovář, M.; Klásek, A.; Kappe, T. *J. Heterocycl. Chem.* **1996**, *33*, 1977–1982.
5. Klásek, A.; Kafka, S. *J. Heterocycl. Chem.* **1998**, *35*, 307–311.
6. (a) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Paladino, G.; Zoni, C. *Eur. J. Org. Chem.* **2005**, 2091–2096; (b) Bergman, J.; Rehn, S. *Tetrahedron* **2002**, *58*, 9179–9185 and references cited therein.
7. (a) Fryer, I. R.; Ning, R. Y.-F.; Sternbach, L. H.; Walser, A. (Hoffmann–La Roche, Inc., USA) U.S. Patent 4,014,883, 1977; *Chem. Abstr.* **1977**, *87*, 39450; (b) Thal, C.; Boye, O.; Guenard, D.; Potier, P. (Centre National de la Recherche Scientifique, Fr.) Patent No. WO 9002733, 1990; *Chem. Abstr.* **1990**, *113*, 115077; (c) Alazard, J.-P.; Millet-Paillusson, C.; Guénard, D.; Thal, C. *Bull. Soc. Chim. Fr.* **1996**, *133*, 251–266; (d) Gorlitzer, K.; Fabian, J.; Frohberg, P.; Drutkowski, G. *Pharmazie* **2002**, *57*, 243–247; (e) Pfefferkorn, J. A.; Song, Y.; Trivedi, B. K. (Warner–Lambert Company LLC, USA), Patent No. WO 2006059210, 2006; *Chem. Abstr.* **2006**, *145*, 45964; (f) Nakahira, H.; Kimura, H.; Hochigai, H. (Dainippon Simitomo Pharma Co., Ltd, Japan) Patent No. WO 2006112331, 2006; *Chem. Abstr.* **2006**, *145*, 454996; (g) Bienayme, H.; Dumoulin, A.; Grisoni, S.; Kaloun, El B.; Poigny, S.; Rabot R.; Rahali, R.; Tam, E. (Pierre Fabre Medicament, Fr.) Patent No. FR 2887881, 2007; *Chem. Abstr.* **2007**, *146*, 121944.
8. It has been reported that bromoacetamides can be prepared from amines and bromoacetyl bromide in THF as a solvent, see, for example: (a) Suzuki, T.; Nagano, Y.; Matsuura, A.; Kohara, A.; Ninomiya, S.; Kohda, K.; Miyata, N. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 4321–4326; (b) Torres-Murro, J.; Quintero, L.; Sartillo-Piscil, F. *Tetrahedron Lett.* **2005**, *46*, 7691–7694.
9. After our experiments in THF were completed, we came across with the work of Schneider and Viljoen who demonstrated how THF reacts with bromoacetyl bromide to afford 4-bromobutyl bromoacetate, see: Schneider, D. F.; Viljoen, M. S. *Synth. Commun.* **2002**, *32*, 721–728.
10. Bestmann, H. J. *Angew. Chem.* **1965**, *77*, 609–613.
11. Podesva, C.; Vagi, K.; Solomon, C. *Can. J. Chem.* **1968**, *46*, 2263–2269.
12. Bonne, D.; Dekhane, M.; Zhu, J. *Org. Lett.* **2005**, *7*, 5285–5288.