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SYNTHESES OF 3-AMINOQUINOLINE-2,4(1*H*,3*H*)-DIONES[#]

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Abstract – Reaction of 3-chloro- (**2**) and 3-bromoquinoline-2,4(1*H*,3*H*)-diones (**3**) with excess of primary alkyl- or arylamines in dimethylformamide provides the corresponding 3-alkyl- or 3-arylamino derivatives (**4**). Compounds (**4**) with the primary amino group at the 3 position were best prepared by reaction of **2** with *in situ* generated ammonia under anhydrous conditions. An alternative approach to the primary amines (**4**) *via* reduction of 3-azidoquinoline-2,4(1*H*,3*H*)-diones (**5**) was investigated. The reduction of **5** with zinc in acetic acid gave moderate to good yields of the desired products, while the reaction with triphenylphosphine afforded exclusively 4-hydroxyquinolin-2(1*H*)-one (**1**).

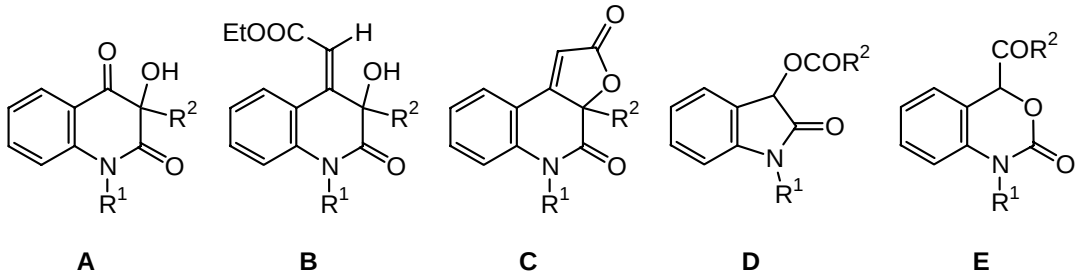
Recently, we have demonstrated interesting chemical transformations of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones (**A**, Chart). For example, Wittig olefination of **A** with ethyl (triphenylphosphoranylidene)acetate proceeded highly stereoselectively to afford *E*-4-ethoxycarbonylmethylene derivatives (**B**).[1] In some cases furo[2,3-*c*]quinoline-2,4(3a*H*,5*H*)-diones (**C**) were obtained, presumably as a result of lactonization of the minor formed *Z*-4-isomer of **B**. The structure of **C** was confirmed by an independent synthesis *via* the intramolecular Wittig reaction.[2] On the other hand, under the same reaction conditions as described for the synthesis of **B**, 5,8-disubstituted 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones (**A**) underwent a completely different reaction, yielding primarily products of indoline (**D**) and benzoxazine (**E**) structural type.[3] Those have been shown to be formed *via* the complex molecular rearrangement of **A**.[4,5]

The diverse and smooth reactivity of 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones (**A**) prompted us to continue similar studies on the closely related 3-aminoquinoline-2,4(1*H*,3*H*)-diones (**4**). So far, few examples of **4** have been reported in the literature. Those include 3-amino-6-chloro-1-methyl-3-phenylquinoline-

[#] *Dedicated to Professor Miloslav Ferles, Professor of Prague Institute of Chemical Technology, on the occasion of his 80th birthday.*

2,4(1*H*,3*H*)-dione, prepared by acid hydrolysis of the corresponding 3-acetamido derivative, which was obtained by a rearrangement of 6-chloro-4-hydroxy-3-imino-1-methyl-4-phenyl-3,4-dihydro-1*H*-quinolin-2-one.[6] In general, ammonolysis of chloro derivatives (**2**) with aqueous ammonia has been shown to yield the corresponding 3-hydroxyquinoline-2,4(1*H*,3*H*)-diones, and only 3-benzyl substituted 3-chloroquinoline-2,4(1*H*,3*H*)-diones (**2**, R^2 = Bn) afforded the desired 3-amino derivative in low yield.[7] Several 3-alkyl- and 3-arylquinoline-2,4(1*H*,3*H*)-diones having tertiary amino group at the 3 position were prepared by the reaction of compound (**2**) or (**3**) with secondary amines.[7,8] To the best of our knowledge, 3-alkyl- or 3-arylquinoline-2,4(1*H*,3*H*)-diones with the secondary amino group at the 3 position (**4**, R^3 = H) have not yet been described. The overall lack of the secondary and especially of the primary amines (**4**) led us to investigate different approaches for their syntheses.

Chart



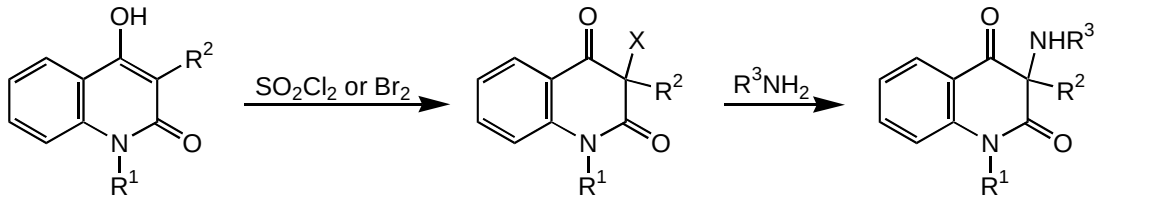
RESULTS AND DISCUSSION

Halides (**2**) and (**3**) can be conveniently prepared by halogenation of **1** with sulfuryl chloride[9,10] or bromine.[9-11] Therefore, the shortest approach to the desired primary and secondary amines (**4**) was considered as a halogen substitution of **2** or **3** with ammonia or primary amines, respectively (Scheme 1). First we examined the reaction of 3-bromo-1-methyl-3-phenylquinoline-2,4(1*H*,3*H*)-dione (**3D**) with a 3-fold excess of primary alkylamines and benzylamine in benzene. Although literature procedures for the amination of halides (**2**) and (**3**) usually require *N*,*N*-dimethylformamide (DMF) as the reaction solvent,[7] we chose benzene because it can be easily removed from the reaction mixture. The aminations proceeded well in refluxing benzene, however, the isolation by evaporation of the volatile compounds resulted in oily materials, from which we were not able to isolate the corresponding amines (**4**). Therefore, the use of this solvent was not pursued further. Aminations conducted in DMF took place at room temperature. The reactions with alkylamines or benzylamine were completed within 24 h, while prolonged reaction times or elevated temperatures were required for sluggish amination of **2** or **3** with aniline. In most cases, a simple workup afforded the corresponding amines (**4**) in 51–92% isolated yield (Table 1). In general and according to expectations, bromo derivatives (**3**) reacted faster than chloro analogues (**2**), however, the latter afford purer products. Therefore, the use of **3** was not always more beneficial, as judged from the

yields of **4** in Table 1.

Next, we employed the above reaction conditions for the synthesis of analogues (**4**) (R^3 = H), having primary amino group at 3 position. We found out that by ammonolysis of **2** or **3** with aqueous ammonia in DMF, only 3-benzyl substituted 3-aminoquinoline-2,4(1*H*,3*H*)-dione (**4**) (R^2 = Bn, R^3 = H) can be prepared, while for the synthesis of other primary 3-alkyl-3-amino and 3-aryl-3-amino analogues (**4**, R^2 = alkyl, aryl, R^3 = H) this protocol cannot generally be applied. These results are consistent with the literature report on the amination of 3-chloroquinoline-2,4(1*H*,3*H*)-diones.[7]

Scheme 1



1
R^1 = H, Me, CH_2Ph, Ph
R^2 = Me, Bu, CH_2Ph, Ph

2 (X = Cl)
3 (X = Br)

4, R^3 = H, Me, Bu, *c*-C_6H_{11}, CH_2Ph, Ph

Another approach that we attempted for the synthesis of primary amines (**4**) involved 3-azidoquinoline-2,4(1*H*,3*H*)-diones (**5**). Literature precedents revealed that 3-chloro compounds (**2**) smoothly reacted with sodium azide to form **5**;[9,12,13] we surmised that **5** would then be easily reduced to the desired **4** (R^3 = H). First, both **2** and **3** were subjected to the reaction with sodium azide. Similarly as described above for the amination, bromo compounds (**3**) reacted faster than chloro analogues (**2**), but also gave significant amounts of by-products, as judged by TLC analysis of the reaction mixture. As demonstrated in Table 2, the isolated yields of purified **5** were comparable, whether **2** or **3** were employed in the reaction.

For the reduction of **5** in the next step we first tried to apply the Staudinger reaction.[14,15] Thus, triphenylphosphine was slowly added to a stirred solution of **5B** (at room temperature or 0 °C), during which a rapid evolution of gas was observed. To our surprise, careful examination of the reaction mixture by TLC showed one spot corresponded in R_f to the authentic 3-benzyl-4-hydroxy-2(1*H*)-quinolone (**1B**), being then isolated from the reaction mixture in 90% yield. It is known that triphenylphosphine can cause debromination of some α-bromo ketones,[16] while deazidation of *α*-azido-*β*-keto esters has been observed under completely different conditions – in a radical chain reaction with tributyltin hydride.[17] To the best of our knowledge, similar deazidation of *α*-azido carbonyl compounds with phosphines has not been described in the literature, but at this point, the reaction was not investigated further.

Similarly to the reaction of azide (**5**) with triphenylphosphine, reduction to **1** was also observed with zinc in cold hydrochloric acid or in boiling acetic acid. Better results with respect to the synthesis of **4** were obtained with zinc and acetic acid, when the reactions were conducted at temperatures below 20 °C. Thus,

besides **1** and some unidentified by-products, compounds (**4**) were formed as major products and were isolated in 21–68% yields (Scheme 2, Table 1).

Table 1. Synthesis of 3-aminoquinoline-2,4(1*H*,3*H*)-diones (**4**).[a]

Product				reaction time[b], yield[c]		
4	R^1	R^2	R^3	from **2**	from **3**	from **5**[d]
4Aa	H	Bu	H	24,[e] 55		0.5, 51
4Ab	H	Bu	Me	24,[e] 72[f]		
4Ac	H	Bu	Bu	3, 92		
4Ad	H	Bu	*c*-C_6H_{11}	24,[e] 81		
4Ae	H	Bu	CH_2Ph	24,[e] 86		
4Ba	H	CH_2Ph	H	24,[e] 62		0.5, 62
4Bb	H	CH_2Ph	Me	6, 52[f]		
4Bc	H	CH_2Ph	Bu	24,[e] 83	24,[e] 92	
4Bd	H	CH_2Ph	*c*-C_6H_{11}	24,[e] 51		
4Be	H	CH_2Ph	CH_2Ph	24,[e] 53		
4Ca	H	Ph	H	18, 53		0.5, 21
4Cb	H	Ph	Me	3.5, 63[f]		
4Cc	H	Ph	Bu	24,[e] 55		
4Cd	H	Ph	*c*-C_6H_{11}	24,[e] 35		
4Ce	H	Ph	CH_2Ph	24,[e] 60		
4Cf[g]	H	Ph	Ph	144,[e] 78		
4Da	Me	Ph	H	24,[e] 92		0.5, 68
4Db	Me	Ph	Me	3, 87[f]		
4Dc	Me	Ph	Bu	24,[e] 90	24,[e] 77	
4Dd	Me	Ph	*c*-C_6H_{11}	24,[e] 68	24,[e] 72	
4De	Me	Ph	CH_2Ph	24,[e] 61		
4Df	Me	Ph	Ph	24,[e] 76		
4Ea	Ph	Me	H	2, 35		
4Eb	Ph	Me	Me	2.5, 70[f]		
4Ec	Ph	Me	Bu	24,[e] 51		
4Ed[g]	Ph	Me	*c*-C_6H_{11}	5, 86		
4Ee[g]	Ph	Me	CH_2Ph	5, 84		
4Ef	Ph	Me	Ph	24,[e] 59		
4Fa	CH_2Ph	Ph	H	24,[e] 30		
4Fb	CH_2Ph	Ph	Me	2, 85[f]		
4Fc	CH_2Ph	Ph	Bu	24,[e] 59		
4Fd	CH_2Ph	Ph	*c*-C_6H_{11}	1.5, 46		
4Fe	CH_2Ph	Ph	CH_2Ph	1.5, 77		
4Ff	CH_2Ph	Ph	Ph	48, 65		

[a] Reactions conducted at room temperature, unless otherwise indicated. [b] Reaction time in h. [c] Refers to isolated percent yield. [d] By reduction with zinc in glacial acetic acid. [e] Non-optimized. [f] Methylamine was *in situ* generated from its HCl salt and K_2CO_3, see EXPERIMENTAL. [g] Isolated as benzene solvate, please see EXPERIMENTAL. [h] Reaction continued for 5 h at 60 °C, and then for 4 h at 80 °C.

Having in mind the easiness of the hydrolysis of halo substituted compounds (**2**) and (**3**), we turned our

attention back to the ammonolysis. We found out that in contrast to the above discussed approaches, the highest yields of primary amines (**4**) (30–92%) can be accessed by reaction of **2** or **3** with ammonia, *in situ* generated from ammonium chloride and potassium carbonate in dimethylformamide, under anhydrous conditions.

In conclusion, we have addressed different approaches for the synthesis of primary and secondary amines (**4**).

Scheme 2

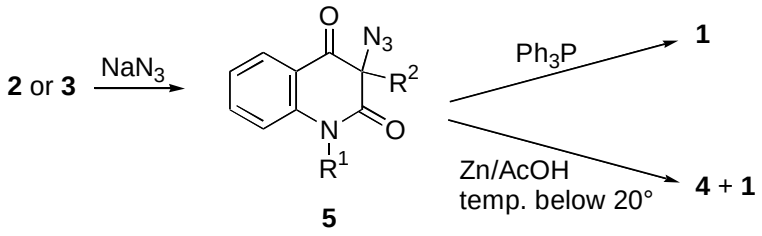


Table 2. Synthesis of 3-azidoquinoline-2,4(1*H*,3*H*)-diones (**5**) from **2** or **3** according to Scheme 2.

Starting compound	X	R^1	R^2	product **5**	yield [*a*]
2	Cl	H	Bu	**5A**	96
2	Cl	H	CH_2Ph	**5B**	93
2	Cl	H	Ph	**5C**	32
2	Cl	Me	Ph	**5D**	93
3	Br	Me	Ph	**5D**	79
2	Cl	Ph	Me	**5E**	75
2	Cl	CH_2Ph	Ph	**5F**	63

[a] Refers to isolated percent yield.

EXPERIMENTAL

Melting points were determined on a Kofler block or Gallenkamp apparatus and are uncorrected. IR spectra were recorded on Perkin-Elmer (421 and 1310) and Mattson 3000 spectrophotometers using samples in potassium bromide disks. NMR spectra were recorded on a Bruker DPX-300 spectrometer in DMSO-d_6 (unless otherwise indicated), with TMS as internal reference. MS spectra were obtained with VG-Analytical AutospecQ instrument. Column chromatography was carried out on silica gel (Kavalier, Votice) using benzene and then successive mixtures of benzene-ethyl acetate (in ratios from 99:1 to 8:2) as eluant (solvent system S). Reactions as well as the course of separation were monitored by TLC on Silufol UV 254 foils (Kavalier, Votice), using benzene-ethyl acetate (4:1) and chloroform-ethanol (9:1) as the eluting systems. Elemental analyses (C, H, N) were performed with Perkin-Elmer 2400 CHN Analyzer and EA 1108 Elemental Analyzer (Fisons Instrument).

Starting 4-hydroxy-2(1*H*)-quinolones (**1**) were prepared by known condensation of anilines with

substituted diethyl malonates as described in the literature.[3,9] Physical and spectroscopic data of compounds (**1A**,[18] **1B**,[18,19] **1C**,[19,20] **1D**,[5,19,20] and **1E**)[5] are published elsewhere.

1-Benzyl-4-hydroxy-3-phenyl-2(1*H*)-quinolone (1F). Colorless crystals, mp 254–255 °C (butanol), yield 78%, lit.,[21] mp 256–258 °C (acetic acid); IR 3036, 2980, 2953, 1620, 1563, 1497, 1455, 1439, 1330, 1310, 1270, 1235, 1170, 1150, 1068, 764, 755, 742, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.57 (s, 2H, CH_2), 6.17 (s, 1H, OH), 7.20-7.34 (m, 7H), 7.40-7.59 (m, 6H), 8.06 (dd, 1H, 5-H, *J* = 8.0, 1.5 Hz). Anal. Calcd for $C_{22}H_{17}NO_2$: C, 80.71; H, 5.23; N, 4.28. Found: C, 81.11; H, 5.31; N, 4.28.

General Procedure for the Synthesis of 3-Chloroquinoline-2,4(1*H*,3*H*)-diones (2). To a stirred suspension of 4-hydroxy-2(1*H*)-quinolone (**1**) (50 mmol) in dioxane (260 mL) preheated to 50 °C, sulfuryl chloride (16.2 g, 120 mmol) was added dropwise, keeping the temperature below 55 °C. The resulting reaction mixture was stirred for additional 10 min at 50–55 °C, cooled down to rt and poured into ice-water (2 L). The precipitated 3-chloroquinoline-2,4(1*H*,3*H*)-dione (**2**) was filtered and washed with water.

3-Butyl-3-chloroquinoline-2,4(1*H*,3*H*)-dione (2A). Yellow crystals, mp 136–138 °C (benzene), yield 97%; IR 3210, 3147, 3089, 3004, 2941, 2870, 1708, 1688, 1611, 1598, 1485, 1439, 1379, 1373, 1361, 1300, 1254, 1156, 1108, 971, 956, 833, 758, 670 cm^{-1}; ^1H NMR δ 0.83 (t, 3H, CH_3, *J* = 7.0 Hz), 1.10-1.33 (m, 4H, 2- and 3-H of butyl), 2.27 (t, 2H, 1-H of butyl, *J* = 7.8 Hz), 7.16 (d, 1H, 8-H, *J* = 7.9 Hz), 7.20 (dt, 1H, 6-H, *J* = 7.7, 0.6 Hz), 7.69 (dt, 1H, 7-H, *J* = 7.7, 1.5 Hz), 7.85 (dd, 1H, 5-H, *J* = 7.8, 1.2 Hz), 11.30 (s, 1H, NH); ^{13}C NMR δ 13.49, 22.11, 26.49, 35.41, 67.00, 116.65, 117.13, 123.31, 127.68, 137.02, 140.95, 166.66, 188.30. Anal. Calcd for $C_{13}H_{14}NO_2Cl$: C, 62.03; H, 5.61; N, 5.56. Found: C, 62.42; H, 5.57; N, 5.44.

3-Benzyl-3-chloroquinoline-2,4(1*H*,3*H*)-dione (2B). Yellow crystals, mp 187–189 °C (ethanol), yield 92%, lit.,[9] mp 181 °C (water-acetic acid).

3-Chloro-3-phenylquinoline-2,4(1*H*,3*H*)-dione (2C). Yellow crystals, mp 178–180 °C (ethanol), yield 89%, lit.,[12] mp 181 °C.

3-Chloro-1-methyl-3-phenylquinoline-2,4(1*H*,3*H*)-dione (2D). Yellow crystals, mp 121–123 °C (ethanol), yield 98%, lit.,[9] mp 154 °C (ethanol).

3-Chloro-3-methyl-1-phenylquinoline-2,4(1*H*,3*H*)-dione (2E). Yellow crystals, mp 195–197 °C (ethanol), yield 90%; IR 3101, 3080, 3073, 3059, 3037, 2994, 2940, 1707, 1677, 1595, 1580, 1492, 1482, 1461, 1436, 1372, 1344, 1303, 1255, 1197, 1158, 1133, 1104, 1071, 1052, 962, 893, 806, 771, 762, 740,

700, 666, 646, 606, 553, 535, 515, 445, 432 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.02 (s, 3H, CH_3), 6.48 (d, 1H, 8-H, *J* = 8.2 Hz), 7.16-7.60 (m, 7H), 8.06 (dd, 1H, 5-H, *J* = 7.7, 1.6 Hz); EIMS m/z(relative intensity) 287(28), 286(16), 285(67), 252(15), 251(68), 250(99), 249(26), 223(25), 222(100), 221(9), 220(14), 196(29), 195(87), 194(15), 167(47), 166(25), 146(33), 139(17), 92(22), 83(18), 81(17), 78(21), 77(59), 76(16). Anal. Calcd for $C_{16}H_{12}NO_2Cl$: C, 67.26; H, 4.23; N, 4.90. Found: C, 67.64; H, 4.03; N, 4.98.

1-Benzyl-3-chloro-3-phenylquinoline-2,4(1*H*,3*H*)-dione (2F). Yellowish crystals, mp 131–133 °C (benzene–cyclohexane), yield 74%; IR 3068, 3052, 2931, 1721, 1687, 1601, 1490, 1464, 1451, 1436, 1370, 1360, 1311, 1270, 1212, 1167, 946, 909, 858, 824, 773, 761, 750, 720, 693, 666, 626, 615, 582, 564, 525, 515, 493, 457, 436 cm^{-1}; ^1H NMR δ 5.32, 5.39 (2d, each, 1H, CH_2, *J* = 16.7 Hz), 7.19-7.43 (m, 12H, 6-H, 8-H, and phenyl protons), 7.60 (ddd, 1H, 7-H, *J* = 8.2, 7.5, 1.7 Hz), 7.93 (dd, 1H, 5-H, *J* = 7.8, 1.7 Hz); ^{13}C NMR δ 46.62, 76.15, 116.38, 120.15, 123.68, 126.43, 127.19, 127.26, 128.02, 128.54, 128.82, 129.45, 134.81, 135.88, 136.51, 140.89, 166.36, 186.99. Anal. Calcd for $C_{22}H_{16}NO_2Cl$: C, 73.03; H, 4.46; N 3.87. Found: C, 73.38; H, 4.35; N, 3.85.

General Procedure for the Preparation of 3-Bromoquinoline-2,4(1*H*,3*H*)-diones (3). To a stirred suspension of 4-hydroxy-2(1*H*)-quinolone (**1**) (20 mmol) in glacial acetic acid (50 mL) at rt, bromine (4.8 g, 30 mmol) was added dropwise during 10 min. The reaction mixture was stirred for 10 min and poured into ice-water (300 mL). The 3-bromoquinoline-2,4(1*H*,3*H*)-dione (**3**) was filtered out and washed with water.

3-Bromo-3-butylquinoline-2,4(1*H*,3*H*)-dione (3A). Yellow crystals, mp 119–123 °C (hexane), yield 93%, lit.,[11] mp 111–113 °C (ethanol).

3-Benzyl-3-bromoquinoline-2,4(1*H*,3*H*)-dione (3B). Yellow crystals, mp 181–184 °C (ethanol), yield 97%, lit.,[11] mp 156–158 °C (ethanol).

3-Bromo-3-phenylquinoline-2,4(1*H*,3*H*)-dione (3C). Yellow crystals, mp 173–175 °C (ethanol), yield 92%, lit.,[9] mp 173 °C (ethanol).

3-Bromo-1-methyl-3-phenylquinoline-2,4(1*H*,3*H*)-dione (3D). Yellow crystals, mp 89–94 °C (ethanol), yield 97%; IR 3077, 3057, 2987, 2939, 2889, 1710, 1682, 1600, 1489, 1471, 1447, 1416, 1345, 1306, 1237, 1172, 1136, 1057, 1039, 960, 900, 801, 775, 750, 700, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.56 (s, 3H, CH_3), 7.23 (dt, 1H, 6-H, *J* = 8.4, 1.5 Hz), 7.30-7.50 (m, 6H, 8-H and phenyl protons), 7.67 (dt, 1H, 7-H, *J* = 7.9, 1.5 Hz), 8.09 (dd, 1H, 5-H, *J* = 7.8, 1.5 Hz). Anal. Calcd for $C_{16}H_{12}NO_2Br$: C, 58.20; H, 3.66; N, 4.24. Found: C, 57.54; H, 3.51; N, 4.48.

3-Bromo-3-methyl-1-phenylquinoline-2,4(1*H*,3*H*)-dione (3E). Yellow crystals, mp 187–190 °C (benzene), yield 79%; IR 3089, 3063, 3044, 3017, 2938, 1703, 1669, 1599, 1492, 1482, 1460, 1438, 1412, 1373, 1344, 1302, 1264, 1256, 1198, 1163, 1132, 1109, 1099, 1071, 1053, 1040, 1024, 1001, 979, 966, 960, 892, 792, 768, 700, 667, 644, 576, 549, 524, 513, 446, 435, 427 cm^{-1}; ^1H NMR δ 2.04 (s, 3H, CH_3), 6.37 (d, 1H, 8-H, *J* = 8.2 Hz), 7.21-7.36 (m, 3H), 7.49-7.64 (m, 4H), 7.99 (dd, 1H, 5-H, *J* = 7.7, 1.6 Hz); ^{13}C NMR δ 20.02, 55.04, 116.29, 118.85, 123.00, 127.62, 128.38, 128.86, 130.08, 135.43, 137.28, 142.67, 167.55, 187.15. Anal. Calcd for $C_{16}H_{12}NO_2Br$: C, 58.20; H, 3.66; N, 4.24. Found: C, 58.56; H, 3.64; N, 4.17.

1-Benzyl-3-bromo-3-phenylquinoline-2,4(1*H*,3*H*)-dione (3F). Yellow crystals, mp 132–135 °C (benzene–cyclohexane), yield 39%,; IR 3089, 3055, 3029, 2972, 2931, 1698, 1670, 1599, 1497, 1489, 1467, 1454, 1443, 1376, 1360, 1322, 1310, 1257, 1220, 1201, 1167, 1155, 1131, 1077, 1028, 1020, 950, 874, 865, 818, 769, 759, 745, 735, 702, 696, 661, 631, 612, 593, 549, 528, 513, 495, 461, 430, 416 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.23, 5.48 (2d, each, 1H, CH_2, *J* = 16.4 Hz), 7.09 (d, 1H, 8-H, *J* = 8.4 Hz), 7.17 (ddd, 1H, 6-H, *J* = 7.6, 7.6, 0.5 Hz), 7.25-7.42 (m, 9H), 7.47-7.53 (m, 3H), 8.10 (dd, 1H, 5-H, *J* = 7.8, 1.6 Hz); ^{13}C NMR ($CDCl_3$) δ 47.32, 76.61, 116.07, 119.92, 123.93, 126.42, 127.68, 128.57, 128.91, 129.02, 129.20, 129.41, 134.03, 135.49, 136.50, 141.33, 167.65, 187.76. Anal. Calcd for $C_{22}H_{16}NO_2Br$: C, 65.04; H, 3.97; N, 3.45. Found: C, 65.29; H, 3.81; N, 3.29.

General Procedure for the Reaction of 2 or 3 with Primary Amines. A mixture of **2** or **3** (5 mmol) in DMF (9 mL) and the appropriate primary amine (15 mmol) was left at rt for the time indicated in Table 1. The resulting mixture was poured into ice-water (100 mL) and the crude product (**4**) was separated and purified, depending on its physical appearance, as follows.

Oily amines (**4Dc**) and (**4De**) were extracted with benzene (3 × 30 mL). The combined extracts were dried over potassium carbonate and evaporated *in vacuo*. The resulting residue was purified by column chromatography using solvent system S.

In the case of **4Fc** the crude oily product was purified as follows. The crude oily product was dissolved in methanol (5 mL), acidified with concentrated hydrochloric acid (2 mL) and the resulting mixture was evaporated to dryness. Thus obtained residue was washed with dry ether (2 × 20 mL) and crystallized repeatedly from isopropyl alcohol affording **4Fc** · HCl (1.310 g, 60%). The hydrochloride **4Fc** · HCl (870 mg, 2.00 mmol) was then suspended in ether (15 mL) and treated with potassium carbonate (553 mg, 4 mmol) and water (1 mL). After the solid material dissolved, the layers were separated, and aqueous layer was extracted with ether (4 × 15 mL). The combined organic layers were dried over potassium carbonate and evaporated *in vacuo*. From the oily residue the amine (**4Fc**) (776 mg, 97% from hydrochloride,

overall yield 59%) slowly crystallized out.

Separation and purification of crystalline amines (**4Ac–e**, **4Bc**–**e**, **4Cc**, **4Ce**, **4Dd**, **4Df**, **4Ec**–**f**, and **4Fd-f**): Precipitated crude amine from the above protocol was filtered off and dissolved in a mixture of benzene (20 mL) and hydrochloric acid (5%, 20 mL). Layers were separated and benzene layer was extracted with hydrochloric acid (5%, 2 × 10 mL). The collected aqueous layers were made alkaline by the addition of concentrated aqueous ammonia. Precipitated amine (**4**) was filtered off, washed with water, and purified by crystallization from the solvent, as indicated below.

In the case of **4Cd** the following workup was necessary to obtain pure product. Precipitated crude amine from the above protocol was filtered off and shortly boiled (while stirred) in a mixture of benzene (25 mL) and hydrochloric acid (2.5%, 60 mL). Some solid material remained undissolved. The resulting mixture was cooled down and filtered. The filter cake was crystallized from ethanol and washed with dry ether affording **4Cd** · HCl (1.15 g, 62%, mp 215–226 °C). A part of thus obtained **4Cd** · HCl (1.00 g) was suspended in aqueous potassium carbonate (15%, 20 mL) and extracted with a mixture of ether (35 mL) and chloroform (35 mL). Layers were separated and aqueous layer was extracted with chloroform (3 × 5 mL). The combined organic layers were evaporated to dryness and the residue was crystallized from benzene to give pure amine (**4Cd**) (507 mg, 56% from hydrochloride, 35% overall).

3-Butyl-3-butylaminoquinoline-2,4(1*H*,3*H*)-dione (4Ac). Colorless crystals, mp 134–136 °C (benzene); IR 3295, 3064, 3047, 2957, 2927, 2854, 1719, 1703, 1676, 1612, 1486, 1441, 1356, 1298, 1246, 1184, 935, 883, 830, 751 cm^{-1}; ^1H NMR δ 0.75 (t, 3H, CH_3 of C-butyl, J = 6.7 Hz), 0.82 (t, 3H, CH_3 of N-butyl, J = 7.1 Hz), 1.05-1.38 (m, 8H), 1.65-1.81 (m, 2H, 1-H of C-butyl), 2.20-2.28 (m, 3H, 3-NH and 1-H of N-butyl), 7.10 (d, 1H, 8-H, J = 7.8 Hz), 7.12 (d, 1H, 6-H, J = 7.8 Hz), 7.61 (dt, 1H, 7-H, J = 7.8, 1.5 Hz), 7.77 (dd, 1H, 5-H, J = 8.2, 1.5 Hz), 10.93 (s, 1H, 1-H); ^{13}C NMR δ 13.56, 13.69, 19.66, 22.11, 24.96, 32.07, 44.00, 72.89, 116.27, 119.13, 122.55, 126.53, 136.21, 141.57, 172.82, 196.44. Anal. Calcd for $C_{17}H_{24}N_2O_2$: C, 70.80; H, 8.39; N 9.71. Found: C, 71.19; H, 8.44; N, 9.67.

3-Butyl-3-cyclohexylaminoquinoline-2,4(1*H*,3*H*)-dione (4Ad). Colorless crystals, mp 190–194 °C (benzene–cyclohexane); IR 3331, 3186, 3065, 2926, 2854, 1706, 1692, 1668, 1609, 1596, 1484, 1372, 1357, 1291, 1230, 1160, 946, 888, 800, 757, 666 cm^{-1}; ^1H NMR δ 0.73 (t, 3H, CH_3 of butyl, J = 7.0 Hz), 0.85-1.60 (m, 14H), 1.65-1.76 (m, 2H), 2.22 (br s, 1H, 3-NH), 2.38-2.48 (m, 1H), 7.08-7.16 (m, 2H, 6- and 8-H), 7.61 (dt, 1H, 7-H, J = 7.7, 1.5 Hz), 7.80 (dd, 1H, 5-H, J = 8.1, 1.5 Hz), 10.95 (s, 1H, 1-H); ^{13}C NMR δ 13.51, 22.13, 24.60, 24.72, 25.31, 33.85, 34.39, 41.16, 52.83, 70.55, 116.35, 118.80, 122.61, 126.62, 136.26, 141.60, 173.27, 196.76. Anal. Calcd for $C_{19}H_{26}N_2O_2$: C, 72.58; H, 8.33; N, 8.91. Found: C, 72.35; H, 8.14; N, 9.11.

3-Benzylamino-3-butylquinoline-2,4-(1*H*,3*H*)-dione (4Ae). Colorless crystals, mp 130–132 °C (cyclohexane); IR 3060, 2859, 2754, 1710, 1699, 1674, 1612, 1488, 1459, 1444, 1365, 1297, 1249, 1217, 1175, 1105, 979, 937, 838, 802, 757, 751, 704, 659 cm^{-1}; ^1H NMR δ 0.76 (t, 3H, CH_3 of butyl, J = 7.0 Hz), 1.09-1.23 (m, 4H, 2- and 3-H of butyl), 1.70-1.88 (m, 2H, 1-H of butyl), 2.67 (br s, 1H, 3-NH), 3.47, 3.53 (2d, each, 1H, $PhCH_2$, J = 12.4 Hz), 7.08-7.36 (m, 7H, 6-H, 8-H, and phenyl protons), 7.62 (dt, 1H, 7-H, J = 7.7, 1.5 Hz), 7.78 (dd, 1H, 5-H, J = 8.1, 1.5 Hz), 10.97 (s, 1H, 1-H); ^{13}C NMR δ 13.58, 22.06, 24.96, 48.51, 73.35, 116.26, 119.19, 122.55, 126.61, 127.91, 128.00, 136.16, 140.39, 141.53, 172.58, 196.09. Anal. Calcd for $C_{20}H_{22}N_2O_2$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.56; H, 6.70; N, 8.92.

3-Benzyl-3-butylaminoquinoline-2,4-(1*H*,3*H*)-dione (4Bc). Colorless crystals, mp 163–166 °C (benzene); IR 3314, 3226, 3191, 3067, 2959, 2924, 1703, 1688, 1665, 1611, 1593, 1484, 1439, 1371, 1288, 1234, 1160, 940, 764, 701 cm^{-1}; ^1H NMR δ 0.81 (t, 3H, CH_3, J = 7.1 Hz), 1.17-1.40 (m, 4H, 2- and 3-H of butyl), 2.18-2.42 (m, 3H, 1-H of butyl and 3-NH), 3.06, 3.11 (2d, each, 1H, CH_2Ph, J = 13.3 Hz), 6.90 (d, 1H, 8-H, J = 8.0 Hz), 6.93-6.98 (m, 2H, 3- and 5-H of phenyl), 7.02 (dt, 1H, 6-H, J = 7.6, 0.5 Hz), 7.06-7.13 (m, 3H, 2-, 4-, and 6-H of phenyl), 7.47 (dt, 1H, 7-H, J = 7.7, 1.4 Hz), 7.68 (dd, 1H, 5-H, J = 7.8, 1.3 Hz), 10.88 (s, 1H, 1-H); ^{13}C NMR δ 13.66, 19.61, 32.00, 43.81, 45.49, 73.45, 116.06, 119.37, 122.41, 126.23, 126.74, 127.66, 129.82, 133.86, 136.11, 141.38, 172.04, 196.25. Anal. Calcd for $C_{20}H_{22}N_2O_2$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.58; H, 6.96; N, 8.30.

3-Benzyl-3-cyclohexylaminoquinoline-2,4-(1*H*,3*H*)-dione (4Bd). Colorless crystals, mp 197–200 °C (benzene); IR 3325, 3229, 3064, 2923, 2853, 1702, 1687, 1666, 1609, 1594, 1484, 1366, 1289, 1159, 761, 700, 666 cm^{-1}; ^1H NMR δ 0.85-1.10 (m, 6H), 1.39-1.62 (m, 5H), 2.43 (br s, 1H, 3-NH), 3.06 (s, 2H, CH_2Ph), 6.84 (d, 1H, 8-H, J = 7.8 Hz), 6.88-6.95 (m, 2H, 3- and 5-H of phenyl), 6.99 (dt, 1H, 6-H, J = 7.8, 0.8 Hz), 7.01-7.09 (m, 3H, 2-, 4-, and 6-H of phenyl), 7.43 (ddd, 1H, 7-H, J = 7.5, 7.4, 1.5 Hz), 7.68 (dd, 1H, 5-H, J = 7.9, 1.5 Hz), 10.84 (s, 1H, 1-H); ^{13}C NMR δ 24.53, 25.27, 33.87, 34.40, 47.46, 52.76, 71.44, 115.99, 119.08, 122.37, 126.25, 126.77, 127.59, 129.77, 133.47, 136.05, 141.28, 172.51, 196.72. Anal. Calcd for $C_{22}H_{24}N_2O_2$: C, 75.83; H, 6.94; N, 8.04. Found: C, 76.09; H, 6.86; N, 8.36.

3-Benzyl-3-benzylaminoquinoline-2,4-(1*H*,3*H*)-dione (4Be). Colorless crystals, mp 192–195 °C (benzene–ethyl acetate); IR 3300, 3223, 3184, 3063, 3027, 2921, 1703, 1688, 1665, 1644, 1609, 1593, 1483, 1371, 1292, 1232, 1159, 1109, 1082, 1031, 941, 917, 761, 748, 701, 667 cm^{-1}; ^1H NMR δ 2.80 (br s, 1H, 3-NH), 3.15 (t, 2H, NCH_2Ph, J = 13.4 Hz), 3.46, 3.54 (each d, each, 1H, CCH_2Ph, J = 12.5 Hz), 6.93 (d, 1H, 8-H, J = 8.0 Hz), 6.97-7.01 (m, 2H, 3- and 5-H of phenyl), 7.04 (dt, 1H, 6-H, J = 7.5, 0.7 Hz), 7.08-7.14 (m, 3H, 2-, 4-, and 6-H of phenyl), 7.18-7.34 (m, 5H, phenyl protons), 7.50 (dt, 1H, 7-H, J = 7.8, 1.4 Hz), 7.69 (dd, 1H, 5-H, J = 7.8, 1.4 Hz), 10.95 (s, 1H, 1-H); ^{13}C NMR δ 45.72, 48.30, 116.09,

119.48, 122.43, 126.33, 126.66, 126.83, 127.64, 127.91, 127.94, 129.93, 133.71, 136.09, 140.10, 141.38, 171.75, 195.84. Anal. Calcd for $C_{23}H_{20}N_2O_2$: C, 77.51; H, 5.66; N, 7.86. Found: C, 77.64; H, 5.37; N, 7.59.

3-Butylamino-3-phenylquinoline-2,4-(1*H*,3*H*)-dione (4Cc). Colorless crystals, mp 123–126 °C (benzene–cyclohexane); IR 3300, 3068, 3052, 3035, 2965, 2924, 2905, 2851, 1716, 1701, 1672, 1614, 1594, 1487, 1446, 1358, 1344, 1317, 1249, 1231, 903, 758. 740, 695, 590, 514, 438 cm^{-1}; ^1H NMR δ 0.85 (t, 3H, CH_3, J = 7.2 Hz), 1.25-1.48 (m, 4H, 2- and 3-H of butyl), 2.36-2.45 (m, 2H, NCH_2), 2.61 (s, 1H, 3-NH), 7.06-7.14 (m, 2H), 7.27-7.36 (m, 3H), 7.36-7.41 (m, 2H), 7.60 (ddd, 1H, 7-H, J = 8.44, 6.98, 1.46 Hz), 7.71 (dd, 1H, 5-H, J = 7.70, 1.29 Hz), 11.23 (s, 1H, 1-H); ^{13}C NMR δ 13.72, 19.71, 32.12, 44.34, 76.47, 116.38, 119.05, 122.84, 126.41, 127.10, 128.38, 128.62, 136.33, 137.92, 141.14, 171.65, 193.89. Anal. Calcd for $C_{19}H_{20}N_2O_2$: C, 74.00; H, 6.54; N, 9.08. Found: C, 73.61; H, 6.33; N, 9.17.

3-Cyclohexylamino-3-phenylquinoline-2,4-(1*H*,3*H*)-dione (4Cd). Colorless crystals, mp 184–188 °C (benzene); IR 3306, 3047, 2975, 2929, 2854, 2757, 2735, 2689, 2668, 1709, 1692, 1669, 1611, 1594, 1507, 1487, 1466, 1444, 1359, 1353, 1324, 1314, 1252, 1230, 1196, 1161, 1135, 1109, 1083, 1053, 1036, 986, 958, 938, 905, 888, 848, 809, 787, 759, 744, 697, 662, 618, 608, 596, 546, 528, 523, 513, 470, 439, 429 cm^{-1}; ^1H NMR δ 0.96-1.17 (m, 5H), 1.40-1.66 (m, 5H), 2.58 (br s, 2H), 7.11 (ddd, 1H, 6-H, J = 7.6, 7.6, 0.8 Hz), 7.16 (d, 1H, 8-H, J = 8.1 Hz), 7.23-7.33 (m, 3H, 2-, 4-, and 6-H of phenyl), 7.36-7.44 (m, 2H, 3- and 5-H of phenyl), 7.62 (ddd, 1H, 7-H, J = 8.2, 7.2, 1.5 Hz), 7.74 (dd, 1H, 5-H, J = 7.8, 1.3 Hz), 11.24 (s, 1H, 1-H); ^{13}C NMR δ 24.82, 25.33, 34.24, 34.61, 53.08, 74.54, 116.49, 118.51, 122.93, 126.30, 127.30, 128.26, 128.54, 136.43, 138.97, 141.22, 172.34, 194.07. Anal. Calcd for $C_{21}H_{22}N_2O_2$: C, 75.42; H, 6.63; N, 8.38. Found: C, 75.69; H, 6.53; N, 8.61.

3-Cyclohexylamino-3-phenylquinoline-2,4(1*H*,3*H*)-dione hydrochloride (4Cd · HCl). Colorless crystals, mp 209–213 °C (ethanol); IR 3300-3700 (br), 3181, 3087, 3054, 3033, 2981, 2938, 2922, 2903, 2857, 1725, 1677, 1611, 1592, 1560, 1503, 1497, 1484, 1454, 1431, 1423, 1384, 1367, 1358, 1327, 1299, 1247, 1229, 1150, 1122, 1091, 1034, 1024, 980, 956, 893, 874, 868, 786, 775, 764, 747, 709, 699, 683, 667, 589, 549, 540, 525, 501, 472, 456, 439 cm^{-1}; ^1H NMR δ 0.99-1.18 (m, 3H), 1.38-1.54 (m, 3H), 1.65-1.82 (m, 4H), 3.45 (dd, 1H, NCH, J = 14.0, 7.0 Hz), 7.20 (ddd, 1H, 6-H, J = 7.5, 7.5 and 0.5 Hz), 7.32 (d, 1H, 8-H, J = 8.1 Hz), 7.51 (s, 5H, phenyl protons), 7.67 (ddd, 1H, 7-H, J = 7.9, 7.6 and 1.4 Hz), 7.86 (dd, 1H, 5-H, J = 7.8 and 1.0 Hz), 9.98 (s, 2H, NH_2^+), 12.18 (s 1H, 1-H). ^{13}C NMR 24.51, 30.44, 30.76, 57.73, 74.44, 117.04, 117.94, 123.84, 127.55, 128.21, 129.56, 130.97, 137.44, 140.52.

3-Benzylamino-3-phenylquinoline-2,4(1*H*,3*H*)-dione (4Ce). Colorless crystals, mp 178–179 °C

(benzene); IR 3312, 3224, 3161, 3096, 3065, 3026, 3001, 2931, 2900, 2867, 2849, 1710, 1699, 1667, 1613, 1593, 1508, 1485, 1441, 1361, 1322, 1270, 1255, 1238, 1225, 1178, 1157, 1110, 1080, 1069, 1034, 1029, 1015, 979, 966, 947, 908, 868, 815, 771, 760, 740, 704, 693, 670, 662, 601, 583, 532, 527, 497, 488, 446, 441 cm^{-1}; ^1H NMR δ 3.01 (dd, 1H, 3-NH, *J* = 7.9, 6.5 Hz), 3.58-3.70 (m, 2H, CH_2), 7.10 (ddd, 1H, 6-H, *J* = 7.6, 7.6, 0.6 Hz), 7.15 (d, 1H, 8-H, *J* = 8.0 Hz), 7.20-7.50 (m, 10H, phenyl protons), 7.60 (ddd, 1H, 7-H, *J* = 9.0, 7.9, 1.5 Hz), 7.74 (dd, 1H, 5-H, *J* = 7.8, 1.3 Hz), 11.29 (s, 1H, 1-H). ^{13}C NMR δ 48.79, 76.62, 116.40, 119.22, 122.86, 126.53, 126.65, 127.14, 127.97, 127.99, 128.57, 128.75, 136.31, 137.55, 140.49, 141.11, 171.43, 193.74. Anal. Calcd for $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.30; N, 8.18. Found: C, 77.47; H, 5.09; N, 8.40.

3-Phenyl-3-phenylaminoquinoline-2,4(1*H*,3*H*)-dione benzene solvate (4Cf · ½C_6H_6). Yellow crystals, mp 139–150 °C (benzene); IR 3383, 3193, 3119, 3066, 2993, 2927, 2872, 2756, 1708, 1667, 1615, 1601, 1502, 1484, 1449, 1437, 1365, 1341, 1312, 1257, 1252, 1231, 1179, 1158, 1109, 1082, 1036, 1021, 1003, 993, 970, 956, 923, 882, 868, 838, 813, 777, 762, 744, 723, 694, 663, 625, 617, 548, 522, 505, 475, 441, 420 cm^{-1}; ^1H NMR δ 6.33 (d, 2H, 2- and 6-H of N-phenyl, *J* = 7.7 Hz), 6.55 (dd, 1H, 4-H of N-phenyl, *J* = 7.3, 7.3 Hz), 6.69 (s, 1H, 3-NH), 7.01 (dd, 2H, 3- and 5-H of N-phenyl, *J* = 8.2, 7.5 Hz), 7.12 (ddd, 1H, 6-H, *J* = 7.5, 7.5, 0.6 Hz), 7.19 (d, 1H, 8-H, *J* = 7.9 Hz), 7.35-7.44 (m, 6H, 2-, 4-, and 6-H of 3-phenyl and ½C_6H_6), 7.45-7.52 (m, 2H, 3- and 5-H of 3-phenyl), 7.63 (ddd, 1H, 7-H, *J* = 8.2, 7.2, 1.5 Hz), 7.76 (dd, 1H, 5-H, *J* = 7.8, 1.4 Hz), 11.40 (s, 1H, 1-H); ^{13}C NMR δ 74.48, 113.73, 116.51, 116.59, 119.14, 122.96, 127.20, 127.40, 128.21 (C_6H_6), 128.40, 128.95, 129.13, 135.54, 136.50, 140.86, 146.05, 170.53, 192.96. Anal. Calcd for $C_{21}H_{16}N_2O_2$ · ½C_6H_6: C, 78.45; H, 5.21; N, 7.62. Found: C, 78.80; H, 5.03; N, 7.77.

3-Phenyl-3-phenylaminoquinoline-2,4(1*H*,3*H*)-dione ethanol solvate (4Cf · EtOH). The compound (**4Cf** · ½C_6H_6) (170 mg, 0.463 mmol) was dissolved in ethanol (2 mL), the solution was acidified with concentrated hydrochloric acid (0.2 mL), and evaporated to dryness. The residue was washed with dry ether (2 mL) and crystallized from ethanol to give yellow crystals, 148.4 mg (86%), mp 125-129 °C; IR 3465 (br), 3331, 3216, 3182, 3149, 3083, 3049, 2972, 2911, 2863, 2753, 1707, 1671, 1601, 1499, 1484, 1449, 1431, 1356, 1313, 1282, 1256, 1227, 1185, 1163, 1110, 1081, 1037, 1002, 993, 964, 925, 908, 901, 881, 871, 843, 834, 814, 789, 768, 749, 742, 722, 699, 682, 668, 661, 616, 534, 509, 490, 436, 415 cm^{-1}; ^1H NMR 1.06 (t, 3H, CH_3, *J* = 7.0 Hz), 3.40-3.49 (m, 2H, CH_2), 4.34 (t, 1H, OH, *J* = 5.1 Hz), 6.32 (d, 2H, 2- and 6-H of N-phenyl, *J* = 7.8 Hz), 6.55 (dd, 1H, 4-H of N-phenyl, *J* = 7.3, 7.3 Hz), 6.68 (s, 1H, 3-NH), 7.01 (dd, 2H, 3- and 5-H of N-phenyl, *J* = 8.3, 7.5 Hz), 7.12 (ddd, 1H, 6-H, *J* = 7.5, 7.5, 0.9 Hz), 7.19 (d, 1H, 8-H, *J* = 8.0 Hz), 7.36-7.45 (m, 3H, 2-, 4-, and 6-H of 3-phenyl), 7.47-7.50 (m, 2H, 3- and 5-H of 3-

phenyl), 7.64 (ddd, 1H, H-7, J = 8.0, 7.5, 1.5 Hz), 7.75 (dd, 1H, H-5, J = 7.8, 1.4 Hz), 11.40 (s, 1H, 1-H); ^{13}C NMR 18.46, 55.95, 74.47, 113.73, 116.51, 116.59, 119.14, 122.96, 127.20, 127.40, 128.41, 128.96, 129.14, 135.54, 136.51, 140.86, 146.05, 170.53, 192.97. Anal. Calcd for $C_{21}H_{16}N_2O_2 \cdot C_2H_6O$: C, 73.78; H, 5.92; N, 7.48. Found: C, 74.15; H, 6.18; N, 7.40.

3-Butylamino-1-methyl-3-phenylquinoline-2,4(1*H*,3*H*)-dione (4Dc). Yellow oil; IR 3328, 3060, 2955, 2928, 2858, 1704, 1666, 1602, 1492, 1470, 1447, 1352, 1303, 1186, 1122, 1112, 1033, 997, 762, 698 cm^{-1}; ^{1}H NMR δ 0.85 (t, 3H, CH_3 of butyl, J = 7.2 Hz), 1.23-1.37 (m, 2H, 3-H of butyl), 1.37-1.51 (m, 2H, 2-H of butyl), 2.30-2.53 (m, 2H, 1-H of butyl), 2.66 (br s, 1H, NH), 3.53 (s, 1H, NCH_3), 7.17 (t, J = 7.4 Hz, 1H, 6-H), 7.23-7.33 (m, 5H, phenyl protons), 7.38 (d, 1H, 8-H, J = 8.3 Hz), 7.69 (dt, 1H, 7-H, J = 7.8, 1.5 Hz), 7.76 (dd, 1H, 5-H, J = 7.7, 1.5 Hz); ^{13}C NMR δ 13.71, 19.70, 29.84, 32.14, 44.31, 77.05, 115.80, 120.56, 123.12, 126.52, 127.28, 128.45, 128.62, 136.23, 137.84, 142.12, 171.15, 192.79. HRMS Calcd for $C_{20}H_{22}N_2O_2$: 322.1681. Found: 322.1691.

3-Cyclohexylamino-1-methyl-3-phenylquinoline-2,4(1*H*,3*H*)-dione (4Dd). Colorless crystals, mp 98–100 °C (hexane); IR 3333, 2959, 2927, 2851, 1702, 1670, 1603, 1490, 1472, 1443, 1355, 1307, 1123, 1113, 1097, 1041, 765, 751, 722, 703, 648 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.05-1.25 (m, 6H), 1.45-1.70 (m, 4H), 1.82 (br s, 1H, NH), 2.59-2.72 (m, 1H), 3.57 (s, 3H, CH_3), 7.11-7.17 (m, 2H, 6- and 8-H), 7.21-7.28 (m, 3H, 2-, 4-, and 6-H of phenyl), 7.34-7.41 (m, 2H, 3- and 5-H of phenyl), 7.58 (dt, 1H, 7-H, J = 7.8, 1.7 Hz), 7.98 (dd, 1H, 5-H, J = 7.9, 1.7 Hz). Anal. Calcd for $C_{22}H_{24}N_2O_2$: C, 75.83; H, 6.94; N, 8.04. Found: C, 76.10; H, 6.86; N, 8.17.

3-Benzylamino-1-methyl-3-phenylquinoline-2,4(1*H*,3*H*)-dione (4De). Yellow oil; IR 3416, 3340, 3059, 3026, 2920, 2850, 1704, 1665, 1601, 1492, 1471, 1352, 1302, 1126, 1109, 1029,783, 761, 698 cm^{-1}; ^{1}H NMR δ 3.54 (s, 3H, NCH_3), 3.58, 3.71 (each d, each, 1H, $PhCH_2$, J = 12.6 Hz), 7.18 (dt, 1H, 6-H, J = 7.5, 0.5 Hz), 7.24 (d, 1H, 8-H, J = 7.2 Hz), 7.27-7.44 (m, 10H, phenyl protons), 7.69 (dt, 1H, 7-H, J = 7.8, 1.6 Hz), 7.79 (dd, 1H, 5-H, J = 7.7, 1.6 Hz); ^{13}C NMR δ 29.96, 48.83, 77.05, 115.83, 120.73, 123.21, 126.62, 126.67, 127.34, 128.01, 128.03, 128.69, 128.80, 136.29, 137.56, 140.50, 142.14, 171.02, 192.78. HRMS Calcd for $C_{23}H_{20}N_2O_2$: 356.1525. Found: 356.1540.

1-Methyl-3-phenyl-3-phenylaminoquinoline-2,4(1*H*,3*H*)-dione (4Df). Colorless crystals, mp 178–181 °C (ethanol); IR 3415, 3048, 3027, 2932, 1708, 1674, 1599, 1499, 1470, 1447, 1350, 1314, 1302, 1262, 1183, 1123, 1115, 1105, 762, 754, 744, 696 cm^{-1}; ^{1}H NMR δ 3.56 (s, 3H, NCH_3), 6.30 (d, 2H, 2- and 6-H of N-phenyl, J = 7.7 Hz), 6.54 (t, 1H, 4-H of N-phenyl, J = 7.3 Hz), 6.70 (s, 1H, NH), 6.99 (t, 2H, 3- and 5-H of N-phenyl, J = 7.5 Hz), 7.21 (dt, 1H, 6-H, J = 7.5, 0.5 Hz), 7.33-7.42 (m, 5H, 3-phenyl

protons), 7.46 (d, 1H, 8-H, *J* = 8.3 Hz), 7.74 (dt, 1H, 7-H, *J* = 7.8, 1.6 Hz), 7.82 (dd, 1H, 5-H, *J* = 7.7, 1.6 Hz); ^{13}C NMR δ 30.17, 74.80, 113.98, 116.12, 116.50, 120.37, 123.33, 127.21, 127.71, 128.35, 128.97, 129.18, 135.63, 136.57, 142.00, 145.93, 170.03, 191.87. Anal. Calcd for $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.30; N, 8.18. Found: C, 76.93; H, 5.17; N, 8.20.

3-Butylamino-3-methyl-1-phenylquinoline-2,4(1*H*,3*H*)-dione (4Ec). Colorless crystals, mp 79–80.5 °C (cyclohexane); IR 3306, 3076, 3059, 2960, 2922, 2870, 2835, 1692, 1659, 1597, 1491, 1457, 1360, 1334, 1298, 1271, 1249, 1192, 1182, 1168, 1161, 1128, 981, 799, 767, 762, 720, 700, 681, 660, 653, 531, 513, 468, 431 cm^{-1}; ^{1}H NMR δ 0.83 (t, 3H, CH_3 of butyl, *J* = 7.1 Hz), 1.21-1.40 (m, 4H), 1.49 (s, 3H, NCH_3), 2.38-2.41 (m, 3H), 6.34 (d, 1H, 8-H, *J* = 8.3 Hz), 7.19 (dd, 1H, 7-H, *J* = 7.5, 7.5 Hz), 7.28-7.44 (m, 2H), 7.45-7.57 (m, 2H), 7.57-7.67 (m, 2H), 7.91 (dd, 1H, 5-H, *J* = 7.7, 1.4 Hz); ^{13}C NMR δ 13.71, 19.70, 24.62, 32.08, 43.76, 69.67, 116.34, 119.60, 122.84, 127.21, 128.67, 129.10, 130.06, 135.61, 137.51, 143.52, 172.55, 194.97. Anal. Calcd for $C_{20}H_{22}N_2O_2$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.29; H, 6.95; N, 8.61.

3-Cyclohexylamino-3-methyl-1-phenylquinoline-2,4(1*H*,3*H*)-dione benzene solvate (4Ed · ⅓C_6H_6). Colorless crystals, mp 125–131 °C (benzene); IR 3343, 3323, 3092, 3074, 3056, 3043, 2995, 2976, 2933, 2907, 2849, 2656, 1703, 1666, 1596, 1582, 1491, 1483, 1459, 1438, 1415, 1363, 1331, 1299, 1274, 1264, 1244, 1206, 1190, 1177, 1158, 1122, 1114, 1106, 1068, 1051, 1042, 1023, 1001, 987, 973, 961, 950, 932, 916, 888, 867, 848, 818, 796, 784, 772, 758, 737, 714, 694, 679, 667, 656, 617, 593, 583, 558, 537, 522, 498, 484, 467, 451, 431 cm^{-1}; ^{1}H NMR δ 0.92-1.13 (m, 6H), 1.42-1.49 (m, 1H), 1.47 (s, 3H, CH_3), 1.56-1.66 (m, 4H), 2.39 (s, 1H, NH), 6.35 (d, 2H, 8-H, *J* = 8.4 Hz), 7.20 (dd, 1H, *J* = 7.5, 7.5 Hz), 7.20-7.30 (m, 1H), 7.30-7.40 (m, 1H), 7.36 (s, 2H, $^1/_3C_6H_6$), 7.49-7.56 (m, 2H), 7.59-7.65 (m, 2H), 7.95 (d, 1H, 5-H, *J* = 7.6 Hz); ^{13}C NMR δ 24.72, 25.32, 25.89, 34.05, 34.56, 52.65, 67.80, 116.41, 119.07, 122.96, 127.46, 128.22 (C_6H_6), 128.70, 129.18, 130.15, 135,78, 137.46, 143.52, 173.10, 195.17. Anal. Calcd for $C_{22}H_{24}N_2O_2 \cdot ⅓C_6H_6$: C, 76.98; H, 7.00; N, 7.48. Found: C, 77.19; H, 7.08; N, 7.62.

3-Benzylamino-3-methyl-1-phenylquinoline-2,4(1*H*,3*H*)-dione benzene solvate (4Ee · ¼C_6H_6). Colorless crystals, mp 115.5–117 °C (benzene); IR 3322, 3061, 3030, 2984, 2930, 2888, 2839, 1709, 1672, 1601, 1584, 1491, 1462, 1452, 1368, 1334, 1313, 1303, 1276, 1250, 1221, 1208, 1196, 1178, 1159, 1128, 1112, 1071, 1046, 1025, 1003, 979, 907, 896, 866, 830, 818, 784, 766, 755, 726, 701, 675, 658, 597, 540, 524, 511, 464, 446 cm^{-1}; ^{1}H NMR δ 1.58 (s, 3H, CH_3), 2.91 (s, 1H, NH), 3.63 (s, 2H, CH_2), 6.35 (d, 1H, 8-H, *J* = 8.3 Hz), 7.17-7.41 (m, 9H), 7.48-7.63 (m, 4H), 7.93 (dd, 1H, 5-H, *J* = 7.7, 1.3 Hz); ^{13}C NMR δ 25.11, 48.34, 70.04, 116.37, 119.71, 122.86, 126.56, 127.23, 127.90, 128.09, 128.21 (C_6H_6), 128.68, 129.13, 130.03, 135.60, 137.53, 140,52, 143.53, 172.46, 194.93. Anal. Calcd for

$C_{23}H_{20}N_2O_2 \cdot ¼C_6H_6$: C, 78.27; H, 5.76; N, 7.45. Found: C, 78.50; H, 5.37; N, 7.21.

3-Methyl-1-phenyl-3-phenylaminoquinoline-2,4(1*H*,3*H*)-dione (4Ef). Colorless crystals, mp 212–215 °C (ethanol); IR 3357, 3109, 3092, 3063, 3051, 3026, 2980, 2967, 2950, 2926, 2863, 1708, 1661, 1599, 1523, 1499, 1492, 1462, 1435, 1371, 1338, 1315, 1296, 1282, 1255, 1206, 1180, 1161, 1130, 1110, 1071, 1048, 1032, 1002, 993, 987, 955, 898, 864, 841, 817, 809, 782, 768, 752, 743, 714, 696, 683, 662, 618, 560, 533, 524, 516, 438, 427 cm^{-1}; ^1H NMR δ 1.72 (s, 3H, CH_3), 6.25 (d, 2H, 8-H, J = 8.0 Hz), 6.46 (d, 1H, J = 8.4 Hz), 6.53 (dd, 1H, 6-H, J = 7.3, 7.3 Hz), 6.69 (s, 1H, NH), 7.00-7.06 (m, 2H), 7.23-7.32 (m, 2H), 7.44-7.66 (m, 5H), 7.98 (dd, 1H, 5-H, J = 7.7, 1.2 Hz); ^{13}C NMR δ 25.96, 67.30, 112.98, 116.24, 116.84, 119.04, 123.26, 127.72, 128.68, 128.86, 129.20, 130.12, 136.30, 137.22, 143.43, 145.58, 171.91, 194.57. Anal. Calcd for $C_{22}H_{18}N_2O_2$: C, 77.18; H, 5.30; N, 8.18). Found: C, 76.89; H, 5.42; N, 7.73.

1-Benzyl-3-butylamino-3-phenylquinoline-2,4(1*H*,3*H*)-dione (4Fc). Colorless crystals, mp 80–84 °C (hexane); IR 3150-3600 (br), 3331, 3060, 3027, 2952, 2927, 2867, 2853, 1709, 1659, 1601, 1488, 1444, 1377, 1376, 1316, 1222, 1180, 1159, 1118, 1054, 1026, 985, 892, 765, 732, 719, 698, 658, 620, 540, 469, 440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3H, CH_3, J = 7.3 Hz), 1.30-1.44 (m, 2H), 1.47-1.64 (m, 2H), 2.37 (br, 1H, NH), 2.48-2.56, 2.63-2.71 (2m, each, 1H, 1-H of butyl), 5.24, 5.49 (2d, each, CH_2 of benzyl, J = 16.3 Hz), 7.00 (d, 1H, 8-H, J = 8.4 Hz), 7.07 (ddd, 1H, 6-H, J = 7.5, 7.5, 0.7 Hz), 7.17-7.44 (m, 11H), 8.00 (dd, 1H, 5-H, J = 7.7, 1.6 Hz); ^{13}C NMR ($CDCl_3$) δ 13.97, 20.40, 32.79, 45.59, 46.85, 115.75, 121.98, 123.44, 126.61, 127.15, 127.52, 128.46, 128.87, 128.94, 135.80, 135.86, 137.22, 141.81, 172.18, 193.65. Anal. Calcd for $C_{26}H_{26}N_2O_2$: C, 78.37; H, 6.58; N, 7.03. Found: C, 78.71; H, 6.59; N, 6.71.

1-Benzyl-3-butylamino-3-phenylquinoline-2,4(1*H*,3*H*)-dione hydrochloride (4Fc · HCl). Colorless crystals, mp 187–192 °C (isopropyl alcohol); IR 3220-3670 (br), 3062, 3021, 2999, 2967, 2933, 2875, 1710, 1678, 1598, 1570, 1493, 1489, 1468, 1453, 1450, 1437, 1371, 1347, 1335, 1319, 1298, 1279, 1250, 1238, 1218, 1201, 1169, 1145, 1091, 1078, 1060, 1038, 1031, 1018, 979, 962, 936, 905, 841, 772, 752, 737, 717, 703, 658, 607, 589, 533, 521, 508, 447, 439; ^1H NMR δ 0.88 (t, 3H, CH_3, J = 7.2 Hz), 1.34 (tq, 2H, 3-H of butyl, J = 7.3, 7.3 Hz), 1.76 (tt, 2H, 2-H of butyl, J = 7.2, 7.2 Hz), 2.94-3.16 (m, 2H, 1-H of butyl), 5.34, 5.44 (2d, each, 1H, CH_2Ph, J = 16.6 Hz), 7.23-7.35 (m, 7H), 7.35-7.43 (m, 2H), 7.43-7.55 (m, 3H), 7.62 (dd, 1H, 7-H, J = 7.7, 7.4 Hz), 7.96 (d, 1H, 5-H, J = 7.4 Hz), 10.32 (br s, 2H, NH_2); ^{13}C NMR δ 13.36, 19.34, 28.27, 45.93, 46.32, 75.69, 116.72, 120.45, 124.25, 126.73, 127.33, 127.72, 128.28, 128.48, 129.54, 131.15, 135.40, 137.11, 140.52, 165.63, 187.82. Anal. Calcd for $C_{26}H_{26}N_2O_2 \cdot HCl$: C, 71.80; H, 6.26; N, 6.44. Found: C, 71.95; H, 6.21; N, 6.61.

1-Benzyl-3-cyclohexylamino-3-phenylquinoline-2,4(1*H*,3*H*)-dione (4Fd). Colorless crystals, mp 134–

137 °C (cyclohexane); IR 3300-3600 (br), 3340, 3085, 3051, 3035, 3001, 2969, 2928, 2917, 2844, 1703, 1669, 1599, 1495, 1488, 1465, 1450, 1428, 1373, 1362, 1309, 1301, 1269, 1254, 1244, 1214, 1197, 1174, 1162, 1106, 1081, 1069, 1058, 1036, 1030, 1007, 964, 941, 933, 916, 903, 883, 856, 847, 797, 777, 762, 751, 738, 706, 697, 664, 617, 586, 550, 527, 519, 512, 482, 462, 432, 418, 412 cm^{-1}; ^1H NMR δ 0.95-1.18 (m, 5H), 1.41-1.71 (m, 5H), 2.61 (s, 1H, NH), 2.71 (s, 1H, H-1 of cyclohexyl), 5.31, 5.55 (2d, each, 1H, NCH_2, *J* = 16.4 Hz), 7.17 (dd, 1H, 6-H, *J* = 7.2, 7.7 Hz), 7.22-7.41 (m, 11H, 8-H and phenyl protons), 7.60 (ddd, 1H, 7-H, *J* = 8.5, 7.2, 1.5 Hz), 7.86 (dd, 1H, *J* = 7.7, 1.5 Hz); ^{13}C NMR δ 24.90, 25.32, 34.46, 34.70, 45.41, 53.24, 75.23, 116.41, 120.35, 123.46, 126.57, 126.64, 127.22, 127.89, 128.49, 128.55, 128.60, 136.21, 136.39, 138.61, 141.23, 172.18, 193.22. Anal. Calcd for $C_{28}H_{28}N_2O_2$: C, 79.22; H, 6.65; N, 6.60. Found: C, 79.46; H, 6.59; N, 6.76.

1-Benzyl-3-benzylamino-3-phenylquinoline-2,4(1*H*,3*H*)-dione (4Fe). Colorless crystals, mp 120–122 °C (cyclohexane); IR 3200-3600 (br), 3317, 3085, 3060, 3026, 3005, 2958, 2921, 2906, 2844, 2807, 1705, 1672, 1598, 1586, 1559, 1540, 1495, 1486, 1466, 1458, 1443, 1364, 1355, 1339, 1322, 1315, 1304, 1263, 1231, 1207, 1200, 1174, 1158, 1116, 1083, 1064, 1047, 1031, 1017, 999, 970, 951, 931, 906, 882, 858, 845, 777, 759, 748, 732, 720, 702, 669, 662, 623, 616, 596, 571, 531, 517, 508, 488, 456, 439, 419 cm^{-1}; ^1H NMR δ 3.08-3.14 (m, 1H, NH), 3.64 (dd, 1H, NCH, *J* = 12.5, 5.4 Hz), 3.75 (dd, 1H, NCH, *J* = 12.4, 8.7 Hz), 5.42 (s, 2H, CH_2), 7.15 (dd, 1H, 6-H, *J* = 7.5, 7.5 Hz), 7.20-7.44 (m, 16H, 8-H and phenyl protons), 7.57 (ddd, 1H, 7-H, *J* = 8.1, 7.5, 1.3 Hz), 7.85 (dd, 1H, 5-H, *J* = 7.7, 1.2 Hz); ^{13}C NMR δ 45.75, 48.89, 77.18, 116.28, 121.22, 123.39, 126.63, 126.66, 126.78, 127.17, 127.58, 128.00, 128.05, 128.59, 128.79, 136.19, 137.27, 140.56, 141.19, 171.43, 192.99. Anal. Calcd for $C_{29}H_{24}N_2O_2$: C, 80.53; H, 5.59; N, 6.48. Found: C, 80.57; H, 5.67; N, 6.31.

1-Benzyl-3-phenyl-3-phenylaminoquinoline-2,4(1*H*,3*H*)-dione (4Ff). Colorless crystals, mp 217–221 °C (benzene); IR 3369, 3086, 3057, 3033, 3004, 2971, 2932, 1708, 1676, 1599, 1495, 1465, 1453, 1446, 1437, 1377, 1362, 1320, 1308, 1260, 1243, 1214, 1179, 1164, 1112, 1080, 1052, 1035, 1006, 1000, 992, 839, 773, 764, 758, 748, 707, 690, 694, 684, 620, 607, 540, 525, 506, 489, 462, 436 cm^{-1}; ^1H NMR δ 5.29, 5.61 (2d, each, 1H, CH_2, *J* = 16.4 Hz), 6.36 (d, 2H, *J* = 7.9 Hz), 6.59 (dd, 1H, *J* = 7.2, 7.1 Hz), 6.82 (s, 1H, NH), 7.04 (dd, 2H, *J* = 7.8, 7.7 Hz), 7.18 (dd, 1H, *J* = 7.5, 7.5 Hz), 7.2-7.5 (m, 12H), 7.63 (dd, 1H, 7-H, *J* = 7.4, 7.4 Hz), 7.88 (dd, 1H, 5-H, *J* = 7.2, 0.7 Hz); ^{13}C NMR δ 45.54, 74.90, 114.14, 116.58, 116.72, 120.76, 123.57, 126.77, 127.22, 127.36, 128.06, 128.21, 128.33, 128.52, 129.02, 129.34, 135.34, 136.08, 136.56, 140.88, 145.89, 170.65, 191.87. Anal. Calcd for $C_{28}H_{22}N_2O_2$: C, 80.36; H, 5.30; N, 6.69. Found: C, 80.23; H, 5.25; N, 6.48.

General Procedure for the Synthesis of 3-Methylaminoquinoline-2,4(1*H*,3*H*)-diones (4Ab, Bb, Cb,

Db, Eb, Fb). To a stirred suspension of methylamine hydrochloride (270 mg, 4 mmol) and powdered potassium carbonate (1.11 g, 8 mmol) in DMF (10 mL), 3-chloroquinoline-2,4(1*H*,3*H*)-dione (**2**) (2 mmol) was added at rt during 30 min. The resulting mixture was stirred at rt for the time indicated in Table 1. The reaction mixture was then poured into ice-water (100 mL) and the precipitated product (**4**) was filtered off. From the aqueous phase second part of **4** was obtained by extraction into benzene (4×10 mL). Crystallisation of the combined parts of the crude product (**4**) from the solvents indicated below afforded 3-methylaminoquinoline-2,4(1*H*,3*H*)-diones (**4Ab**, **4Bb**, **4Cb**, **4Db**, **4Eb**, **4Fb**) in the yields as shown in Table 1.

3-Butyl-3-methylaminoquinoline-2,4(1*H*,3*H*)-dione (4Ab). Colorless crystals, mp 107–111 °C (benzene–cyclohexane); IR 3353, 3272, 3186, 3114, 3057, 2992, 2951, 2926, 2867, 1698, 1658, 1612, 1596, 1505, 1485, 1461, 1435, 1371, 1317, 1233, 1159, 1133, 936, 910, 856, 761, 665 cm^{-1}; ^1H NMR δ 0.75 (t, 3H, CH_3 of butyl, J = 6.9 Hz), 1.08-1.21 (m, 4H, 2- and 3-H of butyl), 1.70-1.73 (m, 2H, 1-H of butyl), 2.08 (s, 3H, N-CH_3), 2.47 (s, 1H, 3-NH), 7.07-7.17 (m, 2H, 6- and 8-H), 7.61 (t, 1H, 7-H, J = 7.2 Hz), 7.77 (d, 1H, 5-H, J = 7.4 Hz), 10.92 (s, 1H, 1-H); ^{13}C NMR δ 13.57, 22.10, 25.00, 31.06, 73.63, 116.23, 119.21, 122.53, 126.53, 136.15, 141.53, 172.60, 196.18. Anal. Calcd for $C_{14}H_{18}N_2O_2$: C, 68.27; H, 7.37; N, 11.37. Found: C, 68.07; H, 7.11; N, 11.65.

3-Benzyl-3-methylaminoquinoline-2,4(1*H*,3*H*)-dione (4Bb). Colorless crystals, mp 166–169 °C (ethyl acetate); IR 3340, 3219, 3184, 3069, 2920, 1702, 1689, 1664, 1611, 1593, 1485, 1370, 1290, 1160, 1151, 935, 763, 698 cm^{-1}; ^1H NMR δ 2.08 (s, 3H, CH_3), 2.59 (br s, 1H, 3-NH), 3.04, 3.09 (each d, each, 1H, $PhCH_2$, J = 12.4 Hz), 6.92 (d, 1H, 8-H, J = 8.1 Hz), 6.94-6.98 (m, 2H, 3- and 5-H of phenyl), 7.04 (dt, 1H, 6-H, J = 7.5, 0.8 Hz), 7.07-7.15 (m, 3H, 2-, 4-, and 6-H of phenyl), 7.49 (dt, 1H, 7-H, J = 7.7, 1.5 Hz), 7.69 (dd, 1H, 5-H, J = 7.9, 1.4 Hz), 10.90 (s, 1H, 1-H); ^{13}C NMR δ 30.90, 44.88, 74.18, 116.06, 119.45, 122.43, 126.28, 126.71, 127.64, 129.89, 133.96, 136.08, 141.36, 171.78, 195.83. Anal. Calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 72.96; H, 5.57; N, 10.10.

3-Methylamino-3-phenylquinoline-2,4(1*H*,3*H*)-dione (4Cb). Colorless crystals, mp 189–194 °C (benzene); IR 3357, 3309, 3190, 3118, 3059, 2993, 2964, 2927, 2871, 2799, 2750, 2681, 1702, 1660, 1613, 1592, 1503, 1484, 1459, 1451, 1434, 1413, 1384, 1361, 1337, 1321, 1272, 1250, 1239, 1203, 1193, 1176, 1167, 1160, 1138, 1113, 1084, 1036, 1027, 1004, 996, 970, 963, 950 cm^{-1}; ^1H NMR δ 2.22 (s, 3H, CH_3), 2.91 (s, 1H, 3-NH), 7.09 (dd, 1H, 6-H, J = 7.7, 7.7 Hz), 7.13 (d, 1H, 8-H, J = 8.2 Hz), 7.25-7.41 (m, 5H, phenyl protons), 7.60 (dd, 1H, 7-H, J = 7.7, 8.2 Hz), 7.71 (d, 1H, 5-H, J = 7.7 Hz), 11.24 (s, 1H, 1-H); ^{13}C NMR δ 31.59, 77.15, 116.36, 119.18, 122.82, 126.50, 127.08, 128.40, 128.62, 136.30, 137.70, 141.12, 171.50, 193.83. Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.52; H,

5.04; N, 10.22.

1-Methyl-3-methylamino-3-phenylquinoline-2,4(1*H*,3*H*)-dione (4Db). Colorless crystals, mp 115–118 °C (benzene–cyclohexane); IR 3340, 3330, 3066, 2961, 2808, 1703, 1692, 1660, 1599, 1487, 1470, 1451, 1356, 1299, 1255, 1170, 1105, 980, 770, 756, 742 cm^{-1}; ^1H NMR δ 2.20 (s, 3H, 3-NCH_3), 2.92 (br s, 1H, NH), 3.53 (s, 3H, 1-CH_3), 7.17 (t, 1H, 6-H, *J* = 7.5 Hz), 7.25-7.32 (m, 5H, phenyl protons), 7.38 (d, 1H, 8-H, *J* = 8.4 Hz), 7.69 (ddd, 1H, 7-H, *J* = 8.4, 7.7, 1.6 Hz), 7.76 (dd, 1H, 5-H, *J* = 7.7, 1.6 Hz); ^{13}C NMR δ 29.86, 31.59, 77.69, 115.80, 120.71, 123.14, 126.62, 127.26, 128.50, 128.64, 136.23, 137.65, 142.13, 170.99, 192.79. Anal. Calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 73.22; H, 5.78; N, 9.95.

1-Methyl-3-methylamino-1-phenylquinoline-2,4(1*H*,3*H*)-dione (4Eb). Colorless crystals, mp 153–155 °C (benzene); IR 3336, 3091, 3042, 2989, 2974, 2945, 2860, 2798, 1697, 1664, 1598, 1594, 1493, 1482, 1456, 1437, 1433, 1420, 1417, 1365, 1360, 1336, 1304, 1276, 1272, 1250, 1214, 1190, 1172, 1161, 1151, 1108, 1075, 1048, 1043, 1026, 1023, 1002, 977, 907, 843, 816, 800, 771, 748, 734, 700, 680, 669, 658, 646, 518, 487, 448, 432 cm^{-1}; ^1H NMR δ 1.47 (s, 3H, CCH_3), 2.17 (s, 3H, NCH_3), 2.67 (s, 1H, NH), 6.34 (d, 1H, 8-H, *J* = 8.3 Hz), 7.18 (dd, *J* = 7.4, 7.4 Hz, 1H, 6-H), 7.34-7.64 (m, 6H, 7-H and phenyl protons), 7.91 (dd, 1H, 5-H, *J* = 7.6, 0.9 Hz); ^{13}C NMR δ 23.34, 30.73, 69.89, 116.31, 119.69, 122.81, 127.18, 128.67, 129.13, 130.05, 135.53, 137.55, 143.51, 172.25, 194.67. Anal. Calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 73.06; H, 5.63; N, 9.72.

1-Benzyl-3-methylamino-3-phenylquinoline-2,4(1*H*,3*H*)-dione (4Fb). Colorless crystals, mp 120–124 °C (cyclohexane); IR 3300-3600 (br), 3359, 3055, 3029, 2980, 2951, 2927, 2852, 2792, 1771, 1707, 1671, 1598, 1494, 1488, 1465, 1456, 1446, 1371, 1361, 1314, 1270, 1212, 1180, 1163, 1111, 1080, 1027, 969, 959, 901, 762, 738, 698, 601, 532, 457, 440 cm^{-1}; ^1H NMR δ 2.27 (s, 3H, CH_3), 3.04 (s, 1H, NH), 5.29-5.51 (m, 2H, CH_2), 7.14 (dd, 1H, 6-H, *J* = 7.5, 7.5 Hz), 7.20-7.38 (m, 11H, 8-H and phenyl protons), 7.57 (dd, 1H, 7-H, *J* = 7.4, 7.4 Hz), 7.82 (d, 1H, 5-H, *J* = 7.5 Hz); ^{13}C NMR δ 31.66, 45.55, 77.68, 116.26, 121.15, 123.37, 126.56, 126.74, 127.16, 127.55, 128.60, 128.67, 136.18, 137.39, 141.13, 171.44, 192.96. Anal. Calcd for $C_{23}H_{20}N_2O_2$: C, 77.51; H, 5.66; N, 7.86. Found: C, 77.51; H, 5.80; N, 7.52.

General Procedure for the Synthesis of Primary Amines (4Aa, 4Ba, 4Ca, 4Da, 4Ea, 4Fa) with *in situ* Generated Ammonia. Powdered potassium carbonate (1.11 g, 8 mmol) was added portionwise to a stirred suspension of ammonium chloride (214 mg, 4 mmol) in DMF (10 mL) under cooling with ice-bath during 5 min. To the resulting stirred and cooled mixture a solution of **2** (2 mmol) in DMF (10 mL) was added dropwise during 30 min. The stirring was continued at rt for the time indicated in Table 1 and then

worked-up, depending on the product (**4**)**,** as follows.

- **4Aa**: The above obtained reaction mixture was poured into ice-water and filtered. The filtrate was repeatedly extracted with benzene until the extract was free of the product. The extract was dried, filtered, and evaporated to dryness. The residue was dissolved in a mixture of benzene (20 mL) and hydrochloric acid (5%, 20 mL). Layers were separated and aqueous layer was made alkaline with concentrated aqueous ammonia. Amine (**4Aa**) was extracted into benzene and the extract was dried over potassium carbonate, and evaporated to dryness.

- **4Ba** and **4Da**: After the above reaction mixture was poured into ice-water a part of the precipitated amine (**4**) was filtered off. From the filtrate, the second part of the amine (**4**) was extracted with benzene (the extract was dried over potassium carbonate and evaporated to dryness). Combined portions of crude amine (**4**) were dissolved in a mixture of benzene (20 mL) and hydrochloric acid (5%, 20 mL). Layers were separated and the aqueous layer was made alkaline with concentrated aqueous ammonia and the precipitated amine (**4**) was filtered off.

- **4Ca** and **4Ea**: The above obtained reaction mixture was poured into ice-water and filtered. The filtrate was repeatedly extracted with benzene until the extract was free of the product (15 × 10 mL and 8×30 mL for **4Ca** and **4Ea**, respectively). The filtrate was dried over potassium carbonate and evaporated to dryness.

- **4Fa**: After the above reaction mixture was poured into ice-water a part of the precipitated amine (**4Fa**) was filtered off. From the filtrate, second part of the amine (**4Fa**) was obtained by extraction into benzene (3×10 mL, the extract was dried over potassium carbonate and evaporated to dryness). Combined portions of thus obtained crude amine (**4Fa**) were purified by column chromatography using solvent system S as eluant.

After the isolation, the crude amines (**4Aa**, **4Ba**, **4Ca**, **4Da**, **4Ea**, and **4Fa**) were crystallized from the solvents indicated below. The yields of the purified products are in Table 1. The physical and analytical data are listed as follows.

3-Amino-3-butylquinoline-2,4(1*H*,3*H*)-dione (4Aa). Colorless crystals, mp 114–116 °C (benzene); IR 3408, 3342, 3237, 2958, 2927, 2863, 1705, 1673, 1612, 1596, 1484, 1450, 1378, 1363, 1314, 1232, 1182, 1156, 1020, 956, 949, 757, 689, 680, 668 cm^{-1}; ^1H NMR δ 0.76 (t, 3H, CH_3, J = 6.9 Hz), 1.08-1.28 (m, 4H, 2- and 3-H of butyl), 1.52-1.71 (m, 2H, 1-H of butyl), 2.10 (br s, 2H, NH_2), 7.09 (d, 1H, 8-H, J = 8.1 Hz), 7.12 (t, 1H, 6-H, J = 7.6 Hz), 7.59 (dt, 1H, 7-H, J = 7.7, 1.5 Hz), 7.74 (dd, 1H, 5-H, J = 7.7, 1.3 Hz), 10.78 (br s, 1H, 1-H); ^{13}C NMR δ 13.64, 21.95, 24.96, 41.64, 68.28, 116.10, 118.47, 122.47, 126.70, 135.77, 141.46, 173.28, 196.11. Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 66.84; H, 6.91; N, 11.82.

3-Amino-3-benzylquinoline-2,4(1*H*,3*H*)-dione (4Ba). Colorless crystals, mp 204–206 °C (methanol), lit.,[7] mp 193–195 °C (ethanol); IR 3391, 3322, 3184, 3059, 2994, 2921, 1702, 1655, 1613, 1594, 1485, 1442, 1399, 1285, 1257, 1231, 1163, 1080, 939, 888, 858, 848, 759, 698 cm^{-1}; ^1H NMR δ 2.09 (s, 2H, NH_2), 2.97 (s, 2H, CH_2Ph), 6.95-7.02 (m, 2H, 3- and 5-H of phenyl), 7.02 (d, 1H, 8-H, *J* = 7.9 Hz), 7.10 (dt, 1H, 6-H, *J* = 7.6, 0.9 Hz), 7.13-7.20 (m, 4H, 6-H, 2-, 4-, and 6-H of phenyl), 7.56 (dt, 1H, 7-H, *J* = 7.7, 1.5 Hz), 7.71 (dd, 1H, 5-H, *J* = 7.8, 1.5 Hz), 10.85 (s, 1H, 1-H); ^{13}C NMR δ 48.16, 69.09, 116.08, 118.59, 122.51, 126.58, 126.77, 127.57, 129.94, 134.12, 135.82, 141.40, 172.23, 195.21.

3-Amino-3-phenylquinoline-2,4(1*H*,3*H*)-dione (4Ca). Colorless crystals, mp 205–208 °C (benzene); IR 3385, 3311, 3189, 3126, 3074, 3056, 2993, 2924, 2869, 1704, 1664, 1613, 1595, 1483, 1453, 1435, 1369, 1319, 1250, 1232, 1192, 1178, 1158, 1112, 1007, 957, 603, 884, 876, 824, 777, 764, 745, 700, 690, 680, 660, 584, 531, 496, 446, 406 cm^{-1}; ^1H NMR δ 2.59 (s, 2H, NH_2), 7.10 (dd, 1H, 6-H, *J* = 7.9, 7.4 Hz), 7.14 (d, 1H, 8-H, *J*= 8.3 Hz), 7.23-7.33 (m, 3H, 2-, 4-, and 6-H of phenyl), 7.36-7.41 (m, 2H, 3- and 5-H of phenyl), 7.60 (ddd, 1H, 7-H, *J* = 8.3, 7.2, 1.3 Hz), 7.70 (dd, 1H, 5-H, *J* = 7.7, 1.1 Hz), 11.13 (s, 1H, 1-H); ^{13}C NMR δ 70.57, 116.33, 118.62, 122.77, 125.47, 127.12, 128.04, 128.63, 136.12, 140.46, 141.36, 172.12, 194.07. Anal. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.55; H, 4.68; N, 10.95.

3-Amino-1-methyl-3-phenylquinoline-2,4(1*H*,3*H*)-dione (4Da). Colorless crystals, mp 132–135 °C (benzene–cyclohexane); IR 3379, 3303, 3071, 3046, 2948, 1701, 1660, 1602, 1490, 1469, 1448, 1357, 1301, 1253, 1190, 1101, 999, 867, 829, 776, 764, 701, 666 cm^{-1}; ^1H NMR δ 2.63 (s, 2H, NH_2), 3.50 (s, 3H, CH_3), 7.18 (t, 1H, 6-H, *J* = 7.5 Hz), 7.22-7.32 (m, 5H, phenyl protons), 7.39 (d, 1H, 8-H, *J* = 8.4 Hz), 7.69 (dt, 1H, 7-H, *J* = 7.8, 1.3 Hz), 7.75 (dd, 1H, 5-H, *J* = 7.3, 1.3 Hz); ^{13}C NMR δ 29.85, 71.13, 115.75, 120.23, 123.09, 125.61, 127.24, 128.10, 128.65, 136.09, 140.57, 142.37, 171.68, 193.30. Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 71.93; H, 5.21; N, 10.35.

3-Amino-3-methyl-1-phenylquinoline-2,4(1*H*,3*H*)-dione (4Ea). Colorless crystals, mp 164–167 °C (benzene–cylohexane); IR 3200-3600 (br), 3378, 3311, 3090, 3065, 2985, 2931, 1709, 1671, 1599, 1494, 1481, 1459, 1368, 1334, 1300, 1241, 1199, 1177, 1161, 1106, 1073, 1025, 1001, 981, 968, 891, 845, 803, 793, 769, 703, 663, 647, 518, 487, 451, 439, 426, 404 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.72 (s, 3H, CH_3), 2.23 (s, 2H, NH_2), 6.47 (d, 1H, 8-H, *J* = 8.2 Hz), 7.13-7.63 (m, 7H, 6-H, 7-H, and phenyl protons), 8.02 (dd, 1H, 5-H, *J* = 7.7, 1.6 Hz); ^{13}C NMR ($CDCl_3$) δ 31.12, 66.19, 76.63, 116.84, 119.60, 123.51, 128.06, 129.13, 135.52, 137.21, 143.63, 173.72, 195.84. Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.17; H, 5.30; N, 10.52. Found: C, 72.57; H, 5.30; N, 10.15.

3-Amino-1-benzyl-3-phenylquinoline-2,4(1*H*,3*H*)-dione (4Fa). Colorless crystals, mp 121–123 °C (cyclohexane); IR 3384, 3309, 3065, 3045, 3024, 2985, 1701, 1664, 1600, 1490, 1464, 1455, 1446, 1368, 1319, 1309, 1251, 1218, 1184, 1168, 1108, 1029, 997, 950, 806, 777, 763, 749, 731, 719, 696, 688, 669, 659, 601, 535, 524, 502, 468, 442, 409 cm^{-1}; ^1H NMR δ 2.72 (s, 2H, NH_2), 5.32, 5.39 (each d, each, 1H, CH_2, *J* = 16.6 Hz), 7.15 (dd, 1H, *J* = 7.5, 7.5 Hz), 7.21-7.33 (m, 11H), 7.57 (ddd, 1H, 7-H, *J* = 8.4, 7.3, 1.6 Hz), 7.82 (dd, 1H, 5-H, *J* = 7.7, 1.6 Hz); ^{13}C NMR δ 45.59, 71.29, 116.21, 120.73, 123.28, 125.77, 126.74, 127.16, 127.53, 128.26, 128.50, 128.72, 136.04, 136.27, 140.43, 141.48, 172.39, 193.46. Anal. Calcd for $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.30; N, 8.18. Found: C, 76.86; H, 5.30; N, 8.04.

General Procedure for the Preparation of 3-Azidoquinoline-2,4(1*H*,3*H*)-diones (5). To a stirred solution of **2** or **3** (10 mmol) in DMF (45 mL), sodium azide (975 mg, 15 mmol) was added in small portions during 0.5 h at rt. The reaction mixture was stirred for additional 1.5 h and then poured into ice-water (200 mL). The precipitated product (**4**) was filtered, washed with water and crystallized from the solvent indicated below.

3-Azido-3-butylquinoline-2,4(1*H*,3*H*)-dione (5A). Colorless crystals, mp 112–114 °C (cyclohexane); IR 3239, 2965, 2937, 2904, 2857, 2106, 1723, 1708, 1689, 1611, 1498, 1482, 1467, 1372, 1360, 1306, 1290, 1271, 1241, 1159, 1151, 1111, 989, 915, 883, 775, 745, 671 cm^{-1}; ^1H NMR δ 0.78 (t, 3H, CH_3, *J* = 7.0 Hz), 1.12-1.28 (m, 4H, 2- and 3-H of butyl), 1.80-1.98 (m, 2H, 1-H of butyl), 7.11 (d, 1H, 8-H, *J* = 8.1 Hz), 7.16 (t, 1H, 6-H, *J* = 7.7 Hz), 7.64 (dt, 1H, 7-H, *J* = 7.7, 1.5 Hz), 7.77 (dd, 1H, 5-H, *J* = 7.8, 1.3 Hz), 11.09 (s, 1H, NH); ^{13}C NMR δ 13.50, 21.56, 25.20, 36.82, 74.70, 116.43, 118.37, 122.91, 126.96, 136.40, 141.19, 168.86, 191.18. Anal. Calcd for $C_{13}H_{14}N_4O_2$: C, 60.45; H, 5.46; N, 21.69. Found: C, 60.30; H, 5.42; N, 21.48.

3-Azido-3-benzylquinoline-2,4(1*H*,3*H*)-dione (5B). Colorless crystals, mp 159–162 °C (ethanol), lit.,[9] mp 151 °C (benzene).

3-Azido-3-phenylquinoline-2,4(1*H*,3*H*)-dione (5C). Colorless crystals, mp 170–172 °C (benzene), lit.,[9] mp 169 °C (toluene).

3-Azido-1-methyl-3-phenylquinoline-2,4(1*H*,3*H*)-dione (5D). Colorless crystals, mp 115–118 °C (ethanol), lit.,[9] mp 128 °C (toluene).

3-Azido-3-methyl-1-phenylquinoline-2,4(1*H*,3*H*)-dione (5E). Colorless crystals, mp 119–120 °C (benzene); IR 3428, 3387, 3346, 3091, 3063, 3044, 3016, 2993, 2971, 2105, 1715, 1685, 1603, 1583, 1491, 1464, 1378, 1333, 1301, 1280, 1248, 1199, 1165, 1127, 1116, 1106, 1069, 1048, 1028, 1003, 984,

976, 928, 881, 845, 804, 783, 766, 753, 739, 721, 693, 674, 661, 612, 549, 536, 514, 465, 431 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.93 (s, 3H, CH_3), 6.49 (d, 1H, 8-H, *J* = 8.4 Hz), 7.19 (dd, 1H, *J* = 7.5, 7.5 Hz), 7.19-7.35 (m, 2H), 7.44 (ddd, 1H, *J* = 8.6, 7.1, 1.6 Hz), 7.49-7.63 (m, 3H), 8.04 (dd, 5-H, 1H, *J* = 7.8, 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 23.44, 70.92, 117.13, 118.94, 123.98, 128.59, 128.75, 129.43, 130.56, 136.30, 136.63, 143.22, 169.66, 191.11. Anal. Calcd for $C_{16}H_{12}N_4O_2$: C, 65.75; H, 4.14; N, 19.17. Found: C, 66.06; H, 3.98; N, 18.85.

3-Azido-1-benzyl-1-phenylquinoline-2,4(1*H*,3*H*)-dione (5F). Colorless crystals, mp 127–129 °C (ethanol); IR 3387, 3064, 3038, 3011, 2971, 2941, 2117, 1707, 1682, 1600, 1489, 1466, 1446, 1374, 1336, 1317, 1300, 1273, 1250, 1220, 1169, 1137, 1053, 1031, 1021, 978, 878, 849, 763, 731, 711, 696, 679, 662, 631, 579, 549, 528, 515, 493, 457, 437 cm^{-1}; ^1H NMR δ 5.29, 5.41 (each d, each, 1H, CH_2, *J* = 16.6 Hz), 7.17-7.20 (m, 2H, 6- and 8-H), 7.24-7.34 (m, 7H), 7.41-7.45 (m, 3H), 7.55 (ddd, 1H, 7-H, *J* = 8.2, 7.5, 1.6 Hz), 7.86 (dd, 1H, *J* = 7.6, 1.5 Hz); ^{13}C NMR δ 46.39, 78.09, 116.33, 120.78, 123.61, 126.71, 126.78, 127.21, 127.53, 128.47, 129.55, 130.14, 132.82, 135.88, 136.24, 140.96, 167.90, 188.64. Anal. Calcd for $C_{22}H_{16}N_4O_2$: C, 71.73; H, 4.38; N, 15.21. Found: C, 71.89; H, 4.36; N, 14.82.

General Procedure for the Reduction of 5 to 4 with Zn/AcOH. To a stirred solution of 3-azidoquinoline-2,4(1*H*,3*H*)-dione (**5**, 5 mmol) in glacial acetic acid (25 mL), zinc dust (1.7 g, 25 mmol) was added portionwise during 1 h under cooling to 20 °C. The reaction mixture was stirred for additional 0.5 h at rt and the precipitate was filtered off. The filtrate was evaporated *in vacuo* to dryness and dissolved in a mixture of benzene (25 mL) and hydrochloric acid (5%, 25 mL). Layers were separated. The aqueous layer was made alkaline with ammonia (10%) and the precipitated product (**4**) was filtered off.

By-product 4-hydroxy-2(1*H*)-quinolone (**1**) can be isolated from the above benzene layer by extraction into aqueous sodium hydroxide and subsequent precipitation from the aqueous layer with concentrated hydrochloric acid.

Reaction of 3-Azido-3-benzylquinoline-2,4(1*H*,3*H*)-dione (5B) with Triphenylphosphine. To a stirred solution of azide (**5B**) (585 mg, 2 mmol) in dichloromethane (50 mL) the solution of triphenylphosphine (787 mg, 3 mmol) in dichloromethane (10 mL) was added dropwise during 20 min at 20 °C. Rapid evolution of nitrogen gas was observed. According to TLC analysis, the reaction mixture consisted of triphenylphosphine, triphenylphosphine oxide and 3-benzyl-4-hydroxy-2(1*H*)-quinolone (**1B**). Compound (**1B**) **(**450 mg, 90%) was isolated by column chromatography using solvent system S.

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