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Transition-Metal-Free C-3 Arylation of Quinoline-4-ones with Arylhydrazines

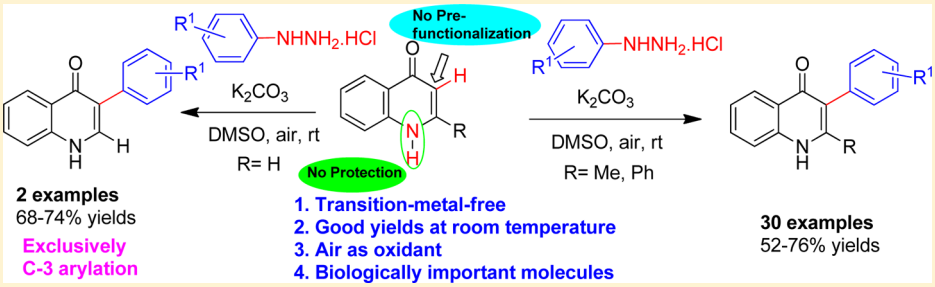
Makthala Ravi,[†,§] Parul Chauhan,[†,§] Ruchir Kant,[‡] Sanjeev K. Shukla,[∥] and Prem. P. Yadav*[,†]

[†]Division of Medicinal and Process Chemistry, CSIR-Central Drug Research Institute, Lucknow 226031, India

[‡]Division of Molecular and Structural Biology, CSIR-Central Drug Research Institute, Lucknow 226031, India

[∥]Sophisticated Analytical Instrument Facility, CSIR-Central Drug Research Institute, Lucknow 226031, India

Supporting Information



ABSTRACT: A transition-metal-free C-3-arylation of quinolin-4-ones in the presence of base has been achieved by using arylhydrazines as aryl radical source and air as oxidant. The reaction proceeds smoothly at room temperature and does not require any prefunctionalization and *N*-protection of quinoline-4-ones. The utility of this methodology is further demonstrated in synthesis of quinoline−quinolone hybrid as well as 6-aryl-benzofuro[3,2-*c*]quinoline scaffold.

Cross-coupling reactions that directly convert C−H to C−C bonds are important synthetic tools for the construction of various biologically important aromatic heterocycles. The transition-metal-catalyzed direct C−H arylation of aromatic heterocycles has been reported extensively.[1] However, they suffer from disadvantages such as toxicity associated with metal impurities in the final product, use of ligands, additives, higher cost, etc. Thus, the development of transition-metal-free C−H arylation processes for the construction of biologically important heterocycles are highly desirable. Radical-mediated functionalization methods would be expected to be a convenient method because of the inherent reactivity of heterocycles toward radical species.[2] In recent years, substantial advances have been made in transition-metal-free C−H arylation processes via radical addition by different aryl sources such as aryl halides,[3] arylboronic acids,[4] diaryliodonium salts,[5] aryldiazonium salts[6] and arylhydrazines.[7] Arylhydrazine derived aryl radicals have found considerable attention in recent past for C−H arylation due to their easy access under oxidative condition, though with very limited substrate scope.[8] Inspired by the recent progress in oxidative phenylhydrazine derived aryl radical addition, we herein report an efficient methodology for C-3 arylation of quinolin-4-ones and its extension toward construction of biologically important aromatic heterocycles.

Our research interest in the synthesis of bioactive heterocyclic molecules[9] and the development of new synthetic methodologies[10] led us to the synthesis of 3-arylated quinolin-4-ones. The quinolin-4-ones are a medicinally important scaffold[11] with molecules under clinical development for malaria. One compound, ELQ-300, is a selective potent inhibitor of the parasite's mitochondrial cytochrome bc1 complex and has been selected as a preclinical candidate for the treatment, prevention and eradication of malaria.[12] Despite the importance of 3-aryl quinoline-4-ones as promising antimalarial agents, arylation at C-3 of quinolin-4-ones remains difficult due to prerequisite *N*-protection and prefunctionalization to generate a better electrophilic partner in the cross-coupling reaction. The synthesis of 3-arylated quinolin-4-ones was described previously in multiple steps either from suitable phenyl substituted precursors[13] or metal mediated arylation at later stages such as Suzuki−Miyaura coupling of *N*-protected 3-halo quinolin-4-ones with aryl boronic acids (Scheme 1a),[14] decarboxylative cross-coupling reaction of *N*-protected quinoline-4-one-3-carboxylic acids with (hetero)aryl halides under a bimetallic system (Scheme 1b)[15] and copper-mediated direct cross-coupling of 3-halo quinolin-4-ones with azoles through C−H functionalization (Scheme 1c).[16] Although such transformations are widely explored, many of these require more than one step, use of transition metals, ligands and high temperature. Therefore, the development of mild, efficient and transition-metal-free processes for C-3 arylation of quinolin-4-ones is required to meet the biological exploration potential of this class of compounds.

Arylhydrazines are known to undergo oxidation in the presence of oxygen to form a highly unstable aryldiazene

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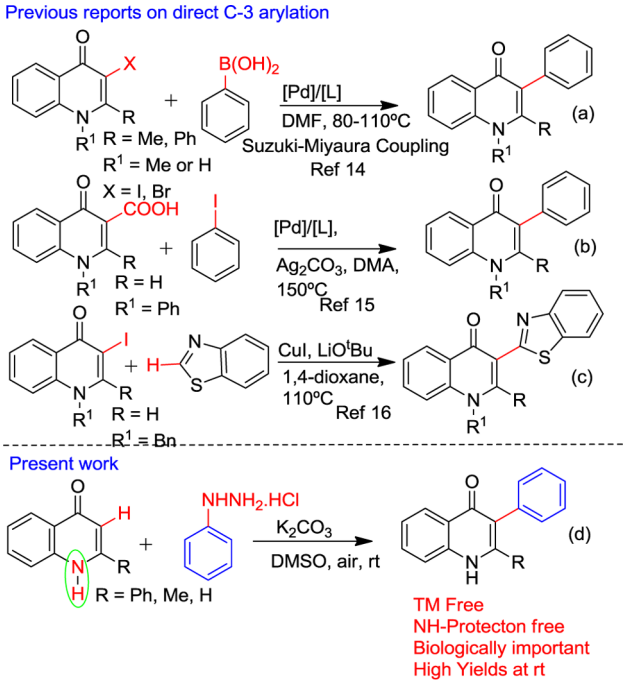
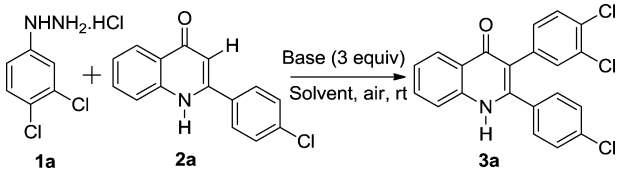
Scheme 1. Strategies for the Synthesis of 3-Aryl Quinolin-4-ones



intermediate that decomposes to N_2 and arenes,[17] this decomposition is even faster under basic conditions. The facile generation of aryl radicals from arylhydrazines and recent reports on the oxidative arylation using arylhydrazines has encouraged us to check the feasibility of the arylation of the C-3 position of the quinolin-4-one moiety. 2-Phenyl substituted quinolin-4-ones were synthesized as per literature procedures in two steps from condensation/aza-cyclization of 2-amino-acetophenone and benzaldehydes followed by oxidation[18,19] and the 2-methyl quinoline-4-one intermediate was synthesized by combining aniline and ethyl acetoacetate via Conrad–Limpach reaction.[20,11]

Our assumption was actualized when 2-(4-chlorophenyl)-quinolin-4-one (**2a**) was reacted with 3,4-dichlorophenylhydrazine (**1a**) in the presence of potassium carbonate in dimethylformamide (DMF) at room temperature for 12 h. To our delight the reaction provided a 30% yield of 3-arylated product **3a** (Table 1, entry 1). Different solvents such as dimethyl sulfoxide (DMSO), dimethylacetamide (DMA) and *N*-methylpyrrolidone (NMP) were screened based on the solubility of the substrate and DMSO found to be the best solvent, providing 76% yield of **3a** (Table 1, entry 2). DMA produced slightly better yields of **3a** than DMF (Table 1, entry 3) whereas in the case of NMP no reaction was observed (Table 1, entry 4). A further set of experiments was conducted to screen the most suitable base for the conversion. Out of the screened bases other than K_2CO_3, i.e, Na_2CO_3, Ag_2CO_3, Cs_2CO_3, NaOH, KOH and KO^{t}Bu, only Ag_2CO_3, Cs_2CO_3 and KOH yielded a >60% yield of product (Table 1, entries 5–10). However, K_2CO_3 produced best yield (Table 1, entry 2). The reaction did not proceed in absence of base (K_2CO_3) even after prolonged reaction time of 36 h, which proved need for base in the reaction (Table 1, entries 11–12). To confirm the need for air as an oxidant, we performed reaction of **1a** and **2a** in dry and degassed DMSO under a nitrogen atmosphere. The desired product **3a** was produced in low yield (22%) indicating that air

Table 1. Optimization of Reaction Conditions for the C-3 Arylation of 2-Aryl Quinolin-4-ones[a]



entry	base	solvent	time (h)	yield[b] (%)
1	K_2CO_3	DMF	12	30
2	**K_2CO_3**	**DMSO**	**12**	**76**
3	K_2CO_3	DMA	12	35
4	K_2CO_3	NMP	12	–
5	Na_2CO_3	DMSO	12	55
6	Ag_2CO_3	DMSO	12	65
7	Cs_2CO_3	DMSO	12	63
8	NaOH	DMSO	12	10
9	KOH	DMSO	12	70
10	KO^{t}Bu	DMSO	12	trace
11	–	DMSO	12	–
12	–	DMSO	36	–
13[c]	K_2CO_3	DMSO	12	22
14[d]	K_2CO_3	DMSO	12	72
15	PIDA	DMSO	12	24
16	I_2	DMSO	12	–
17[e]	TBHP	DMSO	12	–
18	$K_2S_2O_8$	DMSO	12	–

[a]Reaction conditions: **2a** (1.0 mmol), **1a** (1.3 mmol), Base (3.0 mmol), solvent (20 mL) at rt under air. [b]Isolated yields. [c]The reaction was performed in dry and degassed DMSO under nitrogen atmosphere. [d]Under O_2 (balloon). [e]70% aq. TBHP was used.

(O_2) is crucial for the reaction (Table 1, entry 13). The optimized reaction conditions were also tested under O_2 (balloon), which delivered the desired product **3a** in yield similar to that using air (Table 1, entry 14). To check the feasibility of oxidative arylation by other oxidants, we also screened (diacetoxyiodo)benzene (PIDA), *tert*-butyl hydroperoxide (TBHP), $K_2S_2O_8$, and I_2 for this conversion (Table 1, entries 15–18). Among other oxidants, only (diacetoxyiodo)-benzene (PIDA) provided 24% yield of **3a** (Table 1, entry 15); other oxidants were ineffective for this conversion.

With optimal reaction conditions in hand, the scope and generality of this methodology was further investigated with variety of arylhydrazines (**1**) and 2-phenyl-quinolin-4-ones (**2**). Reactions of phenylhydrazines having electron-withdrawing groups such as chloro, bromo, fluoro, cyano and nitro with **2a** afforded 3-arylated product **3a–3g** in good yields (Table 2).[21] Also reaction of hydrazines bearing electron-donating groups such as methoxy and dimethyl with **2a** proceeded smoothly and afforded **3i–3j** in yields of 58–60% (Table 2). The electron-withdrawing and electron-donating groups on 2-phenyl ring were well tolerated and afforded corresponding 3-arylated products in moderate to good yield (Table 2, products **3k–3w**). It was noteworthy that 2-bromo substitution on phenylhydrazine (Table 2, product **3d**) was well tolerated, which is useful for further intramolecular cyclization reactions. Next, we turned our attention toward regioselective arylation of unprotected quinolin-4-one at C-2/C-3 positions. The reaction of quinolin-4-one with arylhydrazines under optimized condition proceeded smoothly and afforded exclusively

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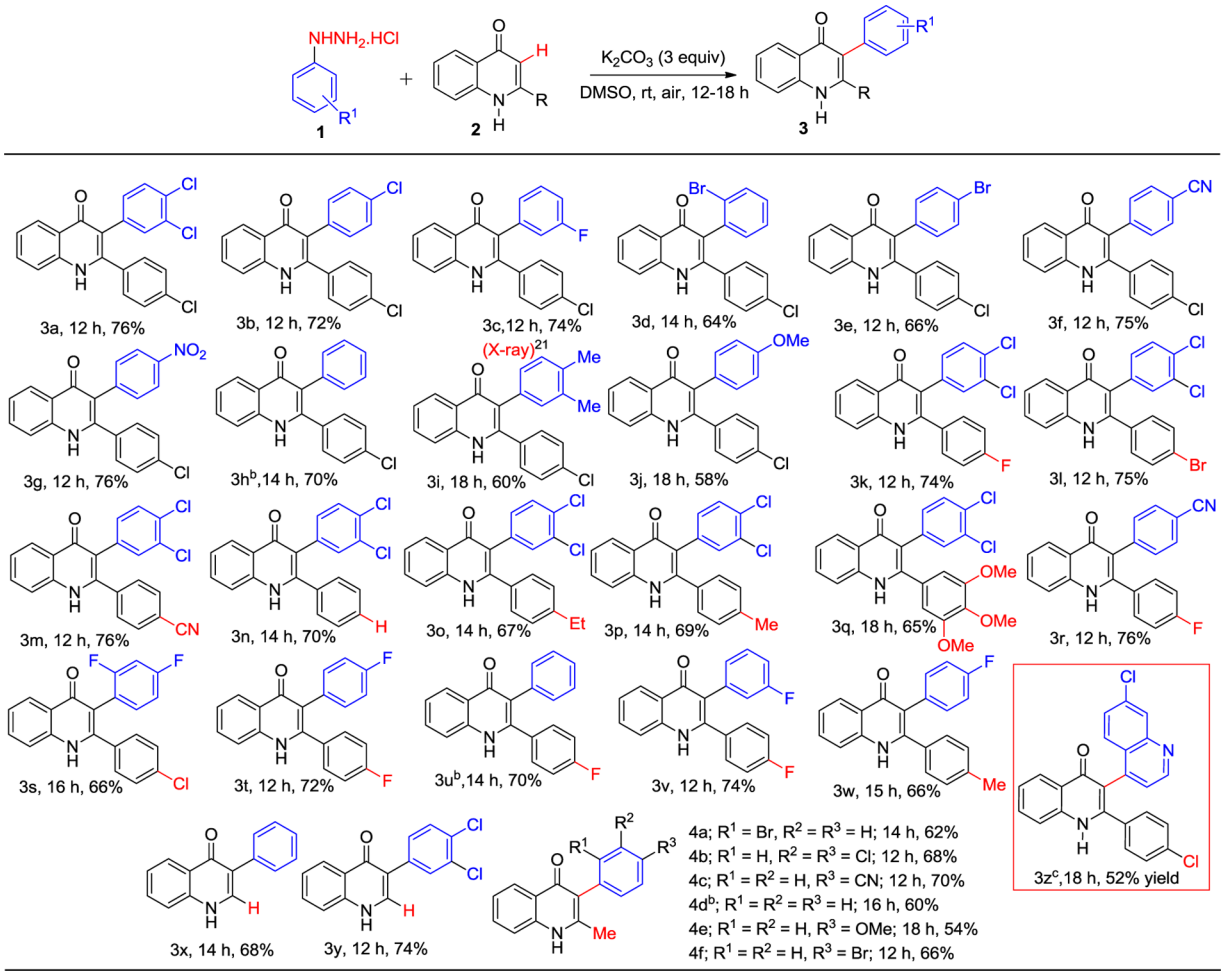
Table 2. Scope of C-3-Arylation of Quinolin-4-ones[a]



[a]Reaction condition: 2 (1.0 mmol), 1 (1.3 mmol), K_2CO_3 (3.0 mmol), DMSO (20 mL) at rt under air. [b]Phenylhydrazine was used as free base. [c]7-Chloro-4-hydrazinylquinoline was used. Time and isolated yields are given.

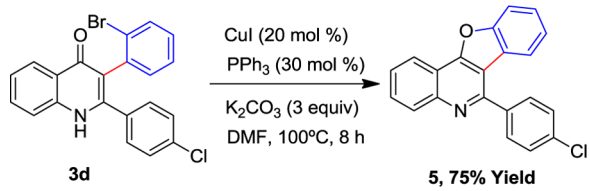
corresponding C-3 arylated products in good yields (Table 2, products **3x** and **3y**).

Molecular hybridization for construction of hybrid molecules with a dual mode of action are gaining importance in medicinal chemistry.[22] To construct such a hybrid, we performed reaction of quinolin-4-one (**2a**) and 7-Chloro-4-hydrazinylquinoline[10] under optimized conditions to afford desired hybrid compound **3z** in moderate yield (Table 2).

Next the optimized methodology was applied to C-3 arylation of 2-methyl substituted quinolin-4-ones, a unique scaffold and key structural unit in antimalarial ELQ-series. We have achieved synthesis of 2-methyl 3-(4-bromophenyl) substituted quinoline-4-one pharmacophore of antimalarial ELQ-271[11c] in good yield (Table 2, product **4f**). Further reaction was extended to synthesis of diverse 2-methyl 3-aryl-quinoline-4-ones in moderate to good yields by reaction of substituted phenylhydrazines with 2-methyl-quinoline-4-one (**2′**) (Table 2, products **4a**–**4e**).

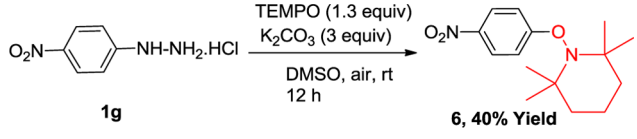
The applicability of 3-arylated quinoline-4-one was further extended to synthesis of benzofuro[3,2-*c*]quinoline skeleton, which has been recently synthesized by Jiang et al.[23] via Pd catalyzed oxidative C–O bond formation. We prepared the 6-phenylbenzofuro[3,2-*c*]quinoline by a Cu promoted intramolecular cyclization of C-3-(2-bromoaryl) product **3d** in 75% yield (Scheme 2).

Scheme 2. Synthesis of 6-Phenylbenzofuro[3,2-*c*]quinoline



To support the radical mechanism, we carried out the radical trapping experiment by using 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) under optimized conditions (Scheme 3), this afforded TEMPO adduct 1-(2,2,6,6-tetramethylpiperidinyloxy)-benzene (**6**). On the basis of our experimental results and previous literature,[8a,17,24–26] we outlined a radical-mediated reaction mechanism as shown in Scheme 4. After formation of the free phenylhydrazine from its hydrochloride salt (**1**) in the

Scheme 3. Radical Trapping Experiment with TEMPO



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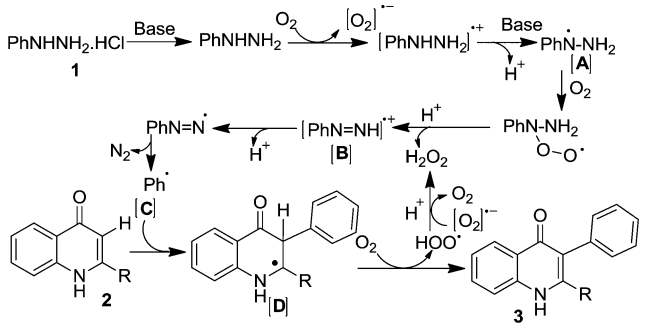
Scheme 4. Plausible Reaction Mechanism



presence of base, it undergoes single electron transfer in the presence of oxygen[28] to form phenylhydrazine cation radical intermediate, which upon simultaneous loss of H^+ in the presence of base leads to phenylhydrazyl radical [**A**]. The radical [**A**] reacts with oxygen to give radical peroxide which further converted into cation radical of phenyldiazene [**B**] and hydrogen peroxide.[24] The unstable cation radical of phenyldiazene rapidly converted into aryl radical [**C**] and N_2 with loss of H^+ and addition of phenyl radical [**C**] with quinoline-4-ones (**2**) gives the intermediate [**D**], which upon oxidation delivered final compound (**3**).[26]

In conclusion, we have developed a mild and efficient protocol for arylhydrazine derived radical mediated C-3 arylation of quinolin-4-ones via denitrogenative coupling of arylhydrazines under mild condition. Also we have successfully achieved synthesis of quinoline-quinolone hybrid as well as 6-aryl-benzofuro[3,2-*c*]quinoline. Operational simplicity without transition metals, no prefunctionalization apart from halogen tolerance, room temperature reaction and good yields are the salient features of present methodology.

EXPERIMENTAL SECTION

General Information. Melting points were determined on a capillary melting point apparatus and are uncorrected. NMR spectra were recorded with 300 and 400 MHz for ^{1}H NMR and 75 and 100 MHz for ^{13}C NMR using DMSO-d_6/$CDCl_3$ as solvent, chemical shift values δ are given in ppm and tetramethylsilane as internal standard. Splitting patterns are described as singlet (s), doublet (d), triplet (t), multiplet (m) and broad (br). HRMS was recorded using Q-TOF mass spectrometer. IR spectra were recorded using FTIR spectrophotometer. Column chromatography was performed over flash silica gel (230−400 Mesh) by smart flash with minimal amount of solvent. All chemicals and reagents were purchased from commercial sources and used without further purification.

General Procedure for 3a−3z and 4a−4f. To a solution of quinolin-4-one (**2**, 1.0 mmol) and phenylhydrazine (**1**, 1.3 mmol) in DMSO (20 mL) was added potassium carbonate (3.0 mmol). The solution was stirred at room temperature under air for 12−18 h. Upon completion, the reaction mixture was diluted with water (100 mL) and extracted with ethyl acetate (2 × 30 mL). The organic layer was further washed with brine solution (3 × 40 mL), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give the crude product. Crude product was further purified by column chromatography over silica gel (hexane/ethyl acetate = 2:1 to 1:1) to afford products **3a−3z** and **4a−4f**.

Synthetic Procedure for 6-(4-Chlorophenyl)benzofuro[3,2-*c*]quinoline (5). To a solution of 3-(2-bromophenyl)-2-(4-chlorophenyl)quinoline-4-one **3d** (0.2 g, 0.488 mmol), CuI (0.018 g, 0.097 mmol) and PPh_3 (0.038 g, 0.146 mmol) in DMF (15 mL) was added potassium carbonate (0.202 g, 1.46 mmol). The solution was stirred at 100 °C for 8 h. Upon completion, the reaction mixture was diluted with water (50 mL) and extracted with ethyl acetate (2 × 20 mL). The organic layer was further washed with brine solution (3 × 30 mL), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give the crude product. Crude product was further purified by column chromatography over silica gel using 5% ethyl acetate−hexane as eluent to furnish 0.120 g (75%) of **5** as white solid.

Radical Trapping Experiment with TEMPO (6). To a solution of 4-nitrophenylhydrazine (0.2 g, 1.31 mmol) and TEMPO (0.306 g, 1.96 mmol) in DMSO (15 mL) was added potassium carbonate (0.542 g, 3.93 mmol). The solution was stirred at room temperature under air for 12 h. Upon completion, the reaction mixture was diluted with water (80 mL) and extracted with ethyl acetate (2 × 20 mL). The organic layer was further washed with brine solution (2 × 30 mL), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give the crude product. Crude product was further purified by column chromatography over silica gel using 1% ethyl acetate−hexane as eluent to furnish 0.145 g (40%) of **6** as white solid.

*2-(4-Chlorophenyl)-3-(3,4-dichlorophenyl)quinolin-4(1H)-one (**3a**).* White solid (304 mg, 76%): mp 350−353 °C; FT-IR (KBr, cm^{-1}) 3410, 3019, 1626; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.95−6.97 (dd, J = 8.28, 2.00 Hz, 1H), 7.37−7.44 (m, 5H), 7.48−7.50 (m, 2H), 7.67−7.73 (m, 2H), 8.15−8.17 (m, 1H), 11.96 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 118.5 (C), 119.0 (CH), 124.1 (CH), 125.1 (C), 125.8 (CH), 128.9 (2 × CH), 129.2 (C), 129.9 (CH), 130.4 (CH), 132.0 (2 × CH), 132.4 (CH), 132.6 (C), 133.9 (C), 134.1 (CH), 134.7 (C), 136.8 (C), 140.0 (C), 148.3 (C), 175.4 (C); ESI-MS (m/z) 400 $(M + H)^+$; HRMS (ESI) calculated for $C_{21}H_{13}Cl_3NO$ $(M + H)^+$ 400.0063, found 400.0056.

*2,3-Bis(4-chlorophenyl)quinolin-4(1H)-one (**3b**).* Light brown solid (264 mg, 72%): mp >385 °C; FT-IR (KBr, cm^{-1}) 3408, 3019, 1625; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.07−7.09 (dd, J = 6.56, 1.92 Hz, 2H), 7.25 (d, J = 8.52 Hz, 2H), 7.35−7.39 (m, 3H), 7.44−7.47 (m, 2H), 7.67−7.72 (m, 2H), 8.16 (d, J = 7.84 Hz, 1H), 11.87 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 118.9 (CH), 119.7 (C), 123.9 (CH), 125.1 (C), 125.8 (CH), 127.9 (2 × CH), 128.7 (2 × CH), 131.3 (C), 131.9 (2 × CH), 132.5 (CH), 133.9 (2 × CH), 134.2 (C), 134.4 (C), 134.9 (C), 140.1 (C), 147.9 (C), 175.6 (C); ESI-MS (m/z) 366 $(M + H)^+$; HRMS (ESI) calculated for $C_{21}H_{14}Cl_2NO$ $(M + H)^+$ 366.0452, found 366.0439.

*2-(4-Chlorophenyl)-3-(3-fluorophenyl)quinolin-4(1H)-one (**3c**).* White solid (258 mg, 74%): mp 352−354 °C; FT-IR (KBr, cm^{-1}) 3410, 3019, 1613; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.82 (d, J = 7.08 Hz, 1H), 6.96 (d, J = 9.36 Hz, 2H), 7.19 (d, J = 6.6 Hz, 1H), 7.37−7.46 (m, 5H), 7.69 (s, 2H), 8.16 (d, J = 7.72 Hz, 1H), 11.89 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 113.6 (d, J = 20.69 Hz, CH), 118.9 (CH), 119.0 (d, J = 20.85 Hz, CH), 119.8 (C), 123.9 (CH), 125.1 (C), 125.8 (CH), 128.3 (CH), 128.7 (2 × CH), 129.6 (d, J = 8.31 Hz, CH), 131.9 (2 × CH), 132.5 (CH), 134.1 (C), 134.4 (C), 138.5 (d, J = 8.46 Hz, C), 140.1 (C), 148.1 (C), 163.5 (d, J = 240.35 Hz, C−F), 175.5 (C); ESI-MS (m/z) 350 $(M + H)^+$; HRMS (ESI) calculated for $C_{21}H_{14}ClFNO$ $(M + H)^+$ 350.0748, found 350.0762.

*3-(2-Bromophenyl)-2-(4-chlorophenyl)quinolin-4(1H)-one (**3d**).* White solid (262 mg, 64%): mp 336−339 °C; FT-IR (KBr, cm^{-1}) 3412, 3019, 1603; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.11−7.17 (m, 2H), 7.21−7.25 (m, 1H), 7.36−7.40 (m, 3H), 7.43−7.45 (m, 2H), 7.54−7.56 (dd, J = 7.9, 1.1 Hz, 1H), 7.69−7.72 (m, 2H), 8.14−8.16 (m, 1H), 11.92 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 118.9 (CH), 121.2 (C), 123.9 (CH), 124.9 (C), 125.8 (CH), 126.4 (C), 127.6 (CH), 128.6 (2 × CH), 129.3 (CH), 131.2 (2 × CH), 132.3 (CH), 132.5 (C), 133.9 (C), 134.2 (CH), 134.6 (C), 137.6 (C), 140.3 (C), 147.9 (C), 175.1 (C); ESI-MS (m/z) 410 $(M + H)^+$; HRMS (ESI) calculated for $C_{21}H_{14}BrClNO$ $(M + H)^+$ 409.9947, found 409.9950.

*3-(4-Bromophenyl)-2-(4-chlorophenyl)quinolin-4(1H)-one (**3e**).* White solid (271 mg, 66%): mp 366−369 °C; FT-IR (KBr, cm^{-1}) 3411, 3019, 1603; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.02 (d, J = 8.4 Hz, 2H), 7.36−7.39 (m, 5H), 7.46 (d, J = 8.48 Hz, 2H), 7.68−7.69 (m, 2H), 8.15 (d, J = 8.16 Hz, 1H), 11.87 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 118.9 (CH), 119.7 (C), 119.9 (C), 123.9 (CH), 125.1 (C), 125.8 (CH), 128.8 (2 × CH), 130.8 (2 × CH), 131.9 (2 ×

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CH), 132.5 (CH), 134.2 (C), 134.3 (2 × CH), 134.5 (C), 135.3 (C), 140.1 (C), 147.9 (C), 175.6 (C); ESI-MS (m/z) 410 $(M + H)^+$; HRMS (ESI) calculated for $C_{21}H_{14}BrClNO$ $(M + H)^+$ 409.9947, found 409.9946.

*4-(2-(4-Chlorophenyl)-4-oxo-1,4-dihydroquinolin-3-yl)-benzonitrile (**3f**).* White solid (267 mg, 75%): mp 383−385 °C; FT-IR (KBr, cm^{-1}) 3421, 3019, 2231, 1644; ^1H NMR (400 MHz, DMSO-d_6) δ 7.27−7.29 (m, 2H), 7.36−7.41 (m, 3H), 7.45−7.47 (m, 2H), 7.65−7.72 (m, 4H), 8.16−8.18 (m, 1H), 11.98 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 109.2 (C), 119.0 (CH), 119.4 (C), 124.2 (CH), 125.2 (C), 125.8 (CH), 128.8 (2 × CH), 131.6 (2 × CH), 132.0 (2 × CH), 132.6 (CH), 133.2 (2 × CH), 133.8 (C), 134.7 (C), 140.1 (C), 141.6 (C), 148.3 (C), 175.3 (C); ESI-MS (m/z) 357 $(M + H)^+$; HRMS (ESI) calculated for $C_{22}H_{14}ClN_2O$ $(M + H)^+$ 357.0795, found 357.0789.

*2-(4-Chlorophenyl)-3-(4-nitrophenyl)quinolin-4(1H)-one (**3g**).* Brown solid (286 mg, 76%): mp >385 °C; FT-IR (KBr, cm^{-1}) 3409, 3019, 1602, 1546, 1346; ^1H NMR (400 MHz, DMSO-d_6) δ 7.35−7.48 (m, 7H), 7.71 (s, 2H), 8.06 (d, J = 8.04 Hz, 2H), 8.18 (d, J = 7.36 Hz, 1H), 12.03 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 119.0 (C), 119.1 (CH), 122.9 (2 × CH), 124.3 (CH), 125.1 (C), 125.8 (CH), 128.9 (2 × CH), 132.1 (2 × CH), 132.7 (CH), 133.4 (2 × CH), 133.7 (C), 134.8 (C), 140.0 (C), 143.9 (C), 146.0 (C), 148.5 (C), 175.2 (C); ESI-MS (m/z) 377 $(M + H)^+$; HRMS (ESI) calculated for $C_{21}H_{14}ClN_2O_3$ $(M + H)^+$ 377.0693, found 377.0701.

*2-(4-Chlorophenyl)-3-phenylquinolin-4(1H)-one (**3h**).*[14c] White solid (232 mg, 70%): mp 380−382 °C; FT-IR (KBr, cm^{-1}) 3402, 3019, 1632; ^1H NMR (400 MHz, DMSO-d_6) δ 7.05−7.08 (m, 2H), 7.11−7.21 (m, 3H), 7.33−7.42 (m, 5H), 7.67−7.69 (m, 2H), 8.16 (d, J = 7.92, 1H), 11.80 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 118.9 (CH), 121.1 (C), 123.8 (CH), 125.1 (C), 125.8 (CH), 126.6 (CH), 127.8 (2 × CH), 128.6 (2 × CH), 131.9 (2 × CH), 132.2 (2 × CH), 132.3 (CH), 134.2 (C), 134.5 (C), 135.9 (C), 140.1 (C), 147.8 (C), 175.8 (C); ESI-MS (m/z) 332 $(M + H)^+$; HRMS (ESI) calculated for $C_{21}H_{15}ClNO$ $(M + H)^+$ 332.0842, found 332.0843.

*2-(4-Chlorophenyl)-3-(3,4-dimethylphenyl)quinolin-4(1H)-one (**3i**).* White solid (215 mg, 60%): mp 362−363 °C; FT-IR (KBr, cm^{-1}) 3412, 3019, 1625; ^1H NMR (400 MHz, DMSO-d_6) δ 2.11 (s, 3H), 2.15 (s, 3H), 6.66−6.68 (dd, J = 7.64, 1.48 Hz, 1H), 6.92 (t, J = 7.72 Hz, 2H), 7.32−7.36 (m, 3H), 7.41−7.44 (m, 2H), 7.66−7.67 (m, 2H), 8.14 (d, J = 7.96 Hz, 1H), 11.73 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 19.5 (CH_3), 19.9 (CH_3), 118.8 (CH), 121.1 (C), 123.6 (CH), 125.1 (C), 125.8 (CH), 128.6 (2 × CH), 129.0 (CH), 129.4 (CH), 131.9 (2 × CH), 132.2 (CH), 133.2 (C), 133.3 (CH), 134.1 (C), 134.3 (C), 134.7 (C), 135.2 (C), 140.1 (C), 147.5 (C), 175.9 (C); ESI-MS(m/z) 360 $(M + H)^+$; HRMS (ESI) calculated for $C_{23}H_{19}ClNO$ $(M + H)^+$ 360.1155, found 360.1136.

*2-(4-Chlorophenyl)-3-(4-methoxyphenyl)quinolin-4(1H)-one (**3j**).* White solid (209 mg, 58%): mp 372−374 °C; FT-IR (KBr, cm^{-1}) 3409, 3019, 1626; ^1H NMR (400 MHz, DMSO-d_6) δ 3.70 (s, 3H), 6.76 (d, J = 8.80 Hz, 2H), 6.97 (d, J = 8.76 Hz, 2H), 7.33−7.36 (m, 3H), 7.43 (d, J = 8.56 Hz, 2H), 7.66−7.67 (m, 2H), 8.14 (d, J = 8.04 Hz, 1H), 11.74 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 55.3 (CH), 113.3 (2 × CH), 118.8 (CH), 120.6 (C), 123.7 (CH), 125.0 (C), 125.8 (CH), 127.8 (C), 128.6 (2 × CH), 131.9 (2 × CH), 132.2 (CH), 133.2 (2 × CH), 134.1 (C), 134.7 (C), 140.0 (C), 147.6 (C), 157.9 (C), 176.0 (C); ESI-MS (m/z) 362 $(M + H)^+$; HRMS (ESI) calculated for $C_{22}H_{17}ClNO_2$ $(M + H)^+$ 362.0948, found 362.0940.

*3-(3,4-Dichlorophenyl)-2-(4-fluorophenyl)quinolin-4(1H)-one (**3k**).* White solid (284 mg, 74%): mp 330−333 °C; FT-IR (KBr, cm^{-1}) 3408, 3019, 1634; ^1H NMR (400 MHz, DMSO-d_6) δ 6.95−6.98 (dd, J = 8.28, 2 Hz, 1H) 7.26 (t, J = 8.88 Hz, 2H), 7.36−7.46 (m, 5H), 7.68−7.73 (m, 2H), 8.15−8.17 (m, 1H), 11.95 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 115.9 (d, J = 21.7 Hz, 2 × CH), 118.6 (C), 118.9 (CH), 124.1 (CH), 125.1 (C), 125.8 (CH), 129.1 (C), 129.9 (CH), 130.3 (C), 131.5 (C), 132.4 (2 × CH), 132.5 (2 × CH), 134.0 (CH), 136.9 (C), 140.0 (C), 148.6 (C), 164.1 (d, J = 245.5 Hz, C−F), 175.4 (C); ESI-MS (m/z) 384 $(M + H)^+$; HRMS (ESI) calculated for $C_{21}H_{13}Cl_2FNO$ $(M + H)^+$ 384.0358, found 384.0361.

*2-(4-Bromophenyl)-3-(3,4-dichlorophenyl)quinolin-4(1H)-one (**3l**).* Light yellow solid (334 mg, 75%): mp 370−373 °C; FT-IR (KBr, cm^{-1}) 3400, 3018, 1624; ^1H NMR (400 MHz, DMSO-d_6) δ 6.95−6.97 (dd, J = 8.28, 2.00 Hz, 1H), 7.33−7.44 (m, 5H), 7.63 (d, J = 8.40 Hz, 2H), 7.67−7.73 (m, 2H), 8.16 (d, J = 7.8 Hz, 1H), 11.95 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 118.5 (C), 119.0 (CH), 123.4 (C), 124.1 (CH), 125.1 (C), 125.8 (CH), 129.2 (C), 129.9 (CH), 130.4 (C), 131.8 (2 × CH), 132.2 (2 × CH), 132.4 (CH), 132.6 (CH), 134.1 (CH), 134.3 (C), 136.8 (C), 140.0 (C), 148.4 (C), 175.4 (C); ESI-MS (m/z) 443 $(M + H)^+$; HRMS (ESI) calculated for $C_{21}H_{13}BrCl_2NO$ $(M + H)^+$ 443.9558, found 443.9555.

*4-(3-(3,4-Dichlorophenyl)-4-oxo-1,4-dihydroquinolin-2-yl)-benzonitrile (**3m**).* White solid (297 mg, 76%): mp 328−330 °C; FT-IR (KBr, cm^{-1}) 3409, 3011, 2234, 1629; ^1H NMR (400 MHz, DMSO-d_6) δ 6.94−6.97 (dd, J = 8.28, 1.8 Hz, 1H), 7.38−7.43 (m, 3H), 7.61 (d, J = 8.20 Hz, 2H), 7.67−7.74 (m, 2H), 7.90 (d, J = 8.20 Hz, 2H), 8.17 (d, J = 7.96 Hz, 1H), 12.06 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 112.5 (C), 118.67 (C), 118.72 (C), 119.1 (CH), 124.3 (CH), 125.1 (C), 125.8 (CH), 129.4 (C), 130.0 (CH), 130.5 (C), 131.2 (2 × CH), 132.4 (CH), 132.69 (2 × CH), 132.74 (CH), 134.1 (CH), 136.5 (C), 139.6 (C), 140.1 (C), 147.8 (C), 175.4 (C); ESI-MS (m/z) 391 $(M + H)^+$; HRMS (ESI) calculated for $C_{22}H_{13}Cl_2N_2O$ $(M + H)^+$ 391.0405, found 391.0400.

*3-(3,4-Dichlorophenyl)-2-phenylquinolin-4(1H)-one (**3n**).* White solid (256 mg, 70%): mp 355−356 °C; FT-IR (KBr, cm^{-1}) 3400, 3019, 1625; ^1H NMR (400 MHz, DMSO-d_6) δ 6.96−6.99 (dd, J = 8.28, 1.96 Hz, 1H), 7.36−7.42 (m, 8H), 7.70 (d, J = 3.48 Hz, 2H), 8.17 (d, J = 7.96 Hz, 1H), 11.95 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 118.4 (C), 119.0 (CH), 124.0 (CH), 125.1 (C), 125.8 (CH), 128.8 (2 × CH), 128.9 (C), 129.8 (CH), 130.0 (2 × CH), 130.3 (C), 132.46 (CH), 132.53 (CH), 134.0 (CH), 135.1 (C), 137.1 (C), 140.0 (C), 149.5 (C), 175.4 (C); ESI-MS (m/z) 366 $(M + H)^+$; HRMS (ESI) calculated for $C_{21}H_{14}Cl_2NO$ $(M + H)^+$ 366.0452, found 366.0453.

*3-(3,4-Dichlorophenyl)-2-(4-ethylphenyl)quinolin-4(1H)-one (**3o**).* White solid (264 mg, 67%): mp 348−350 °C; FT-IR (KBr, cm^{-1}) 3409, 3019, 1602; ^1H NMR (400 MHz, DMSO-d_6) δ 1.16 (t, J = 7.6 Hz, 3H), 2.59−2.64 (q, J = 7.6 Hz, 2H), 6.96−6.99 (dd, J = 8.32, 2 Hz, 1H), 7.24−7.29 (m, 4H), 7.35−7.41(m, 3H), 7.69 (d, J = 3.44 Hz, 2H), 8.15 (d, J = 8.00 Hz, 1H), 11.88 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 15.9 (CH_3), 28.4 (CH_2), 118.3 (C), 118.9 (CH), 123.9 (CH), 125.0 (C), 125.8 (CH), 128.2 (2 × CH), 128.9 (C), 129.8 (CH), 130.0 (2 × CH), 130.3 (C), 132.4 (2 × CH), 134.0 (CH), 137.2 (C), 140.1 (C), 145.8 (C), 149.6 (C), 175.4 (C); ESI-MS (m/z) 394 $(M + H)^+$; HRMS (ESI) calculated for $C_{23}H_{18}Cl_2NO$ $(M + H)^+$ 394.0765, found 394.0773.

*3-(3,4-Dichlorophenyl)-2-(p-tolyl)quinolin-4(1H)-one (**3p**).* White solid (262 mg, 69%): mp 351−353 °C; FT-IR (KBr, cm^{-1}) 3414, 3019, 1696; ^1H NMR (400 MHz, DMSO-d_6) δ 2.32 (s, 3H), 6.94−6.97 (dd, J = 8.32, 1.96 Hz, 1H), 7.20−7.27 (m, 4H), 7.35−7.41 (m, 3H), 7.69 (d, J = 3.4 Hz, 2H), 8.15 (d, J = 8.04 Hz, 1H), 11.86 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 21.3 (CH_3), 118.3 (C), 118.9 (CH), 123.9 (CH), 125.0 (C), 125.8 (CH), 128.9 (C), 129.3 (2 × CH), 129.8 (CH), 129.9 (2 × CH), 130.3 (C), 132.2 (C), 132.4 (2 × CH), 134.0 (CH), 137.3 (C), 139.5 (C), 140.1 (C), 149.6 (C), 175.4 (C); ESI-MS (m/z) 380 $(M + H)^+$; HRMS (ESI) calculated for $C_{22}H_{16}Cl_2NO$ $(M + H)^+$ 380.0609 found 380.0605.

*3-(3,4-Dichlorophenyl)-2-(3,4,5-trimethoxyphenyl)quinolin-4(1H)-one (**3q**).* Light brown solid (296 mg, 65%): mp 307−309 °C; FT-IR (KBr, cm^{-1}) 3409, 3019, 1625; ^1H NMR (400 MHz, DMSO-d_6) δ 3.64 (s, 6H), 3.66 (s, 3H), 6.68 (s, 2H), 7.02−7.05 (dd, J = 8.28, 2 Hz, 1H), 7.36−7.39 (m, 1H), 7.43−7.47 (m, 2H), 7.69−7.71 (m, 2H), 8.16 (d, J = 7.96 Hz, 1H), 11.90 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 56.4 (2 × CH_3), 60.6 (CH_3), 108.1 (2 × CH), 118.4 (C), 118.9 (CH), 124.0 (CH), 125.1 (C), 125.8 (CH), 129.0 (C), 129.9 (CH), 130.1 (C), 130.3 (C), 132.2 (CH), 132.5 (CH), 133.9 (CH), 137.6 (C), 138.7 (C), 139.9 (C), 149.2 (C), 152.9 (2 × C), 175.4 (C); ESI-MS (m/z) 456 $(M + H)^+$; HRMS (ESI) calculated for $C_{24}H_{20}Cl_2NO_4$ $(M + H)^+$ 456.0769, found 456.0775.

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*4-(2-(4-Fluorophenyl)-4-oxo-1,4-dihydroquinolin-3-yl)-benzonitrile (**3r**).* White solid (258 mg, 76%): mp 368−370 °C; FT-IR (KBr, cm^{-1}) 3430, 3019, 2231, 1609; ^1H NMR (400 MHz, DMSO-d_6) δ 7.20−7.28 (m, 4H), 7.37−7.42 (m, 3H), 7.64−7.66 (m, 2H), 7.69−7.74 (m, 2H), 8.17 (d, J = 7.84 Hz, 1H), 11.97 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 109.1 (C), 115.9 (d, J = 21.75 Hz, 2 × CH), 119.0 (C), 119.5 (CH), 124.1 (CH), 125.1 (C), 125.8 (CH), 131.4 (d, J = 3.27 Hz, C), 131. Six (2 × CH), 132.5 (CH), 132.6 (d, J = 4.5 Hz, 2 × CH), 133.2 (2 × CH), 140.1 (C), 141.8 (C), 148.6 (C), 164.1 (d, J = 245.75 Hz, C−F), 175.3 (C); ESI-MS (m/z) 341 $(M + H)^+$; HRMS (ESI) calculated for $C_{22}H_{14}FN_2O$ $(M + H)^+$ 341.1090, found 341.1089.

*2-(4-Chlorophenyl)-3-(2,4-difluorophenyl)quinolin-4(1H)-one (**3s**).* White solid (242 mg, 66%): mp 352−353 °C; FT-IR (KBr, cm^{-1}) 3412, 3019, 1625; ^1H NMR (400 MHz, DMSO-d_6) δ 6.92−6.97 (m, 1H), 7.06−7.17 (m, 2H), 7.35−7.41 (m, 3H), 7.45−7.47 (m, 2H), 7.68−7.74 (m, 2H), 8.13−8.15 (m, 1H), 11.99 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 103.9 (t, J = 26.3 Hz, CH), 111.2−111.4 (m, CH), 114.3 (C), 119.0 (CH), 120.2−120.4 (m, C), 124.1 (CH), 124.7 (C), 125.7 (CH), 128.8 (2 × CH), 131.3 (2 × CH), 132.6 (CH), 133.8 (C), 134.7 (C), 135.1−135.3 (m, CH), 140.2 (C), 148.9 (C), 159.4−161.9 (dd, J = 245.1, 12.6 Hz, C−F), 160.7−163.2 (dd, J = 244, 11.8 Hz, C−F), 175.4 (C); ESI-MS (m/z) 368 $(M + H)^+$; HRMS (ESI) calculated for $C_{21}H_{13}ClF_2NO$ $(M + H)^+$ 368.0654, found 368.0641.

*2,3-Bis(4-fluorophenyl)quinolin-4(1H)-one (**3t**).* White solid (240 mg, 72%): mp >385 °C; FT-IR (KBr, cm^{-1}) 3411, 3019, 1696; ^1H NMR (400 MHz, DMSO-d_6) δ 7.01 (t, J = 8.92 Hz, 2H), 7.07−7.10 (m, 2H), 7.21 (t, J = 8.84 Hz, 2H), 7.34−7.40 (m, 3H), 7.68 (d, J = 3.44 Hz, 2H), 8.16 (d, J = 8.08 Hz, 1H), 11.83 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 114.7 (d, J = 21.1 Hz, 2 × CH), 115.7 (d, J = 21.55 Hz, 2 × CH), 118.9 (CH), 120.0 (C), 123.8 (CH), 125.1 (C), 125.8 (CH), 131.9 (C), 132.29 (C), 132.34 (CH), 132.5 (d, J = 8.6 Hz, 2 × CH), 134.0 (d, J = 7.9 Hz, 2 × CH), 140.1 (C), 148.2 (C), 162.3 (d, J = 241.5 Hz, C−F), 163.9 (d, J = 245.4 Hz, C−F), 175.8 (C); ESI-MS (m/z) 334 $(M + H)^+$; HRMS (ESI) calculated for $C_{21}H_{14}F_2NO$ $(M + H)^+$ 334.1043, found 334.1044.

*2-(4-Fluorophenyl)-3-phenylquinolin-4(1H)-one (**3u**).*[14c] White solid (220 mg, 70%): mp 382−383 °C; FT-IR (KBr, cm^{-1}) 3408, 3019, 1606; ^1H NMR (400 MHz, DMSO-d_6) δ 7.05−7.07 (m, 2H), 7.10−7.19 (m, 5H), 7.33−7.39 (m, 3H), 7.68−7.69 (m, 2H), 8.16 (d, J = 8.00 Hz, 1H), 11.79 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 115.6 (d, J = 21.54 Hz, 2 × CH), 118.9 (CH), 121.1 (C), 123.7 (CH), 125.1 (C), 125.8 (CH), 126.5 (CH), 127.8 (2 × CH), 132.1 (d, J = 3.18 Hz, C), 132.2 (2 × CH), 132.26 (CH), 132.34 (CH), 132.4 (CH), 136.1 (C), 140.1 (C), 148.0 (C), 163.9 (d, J = 245.6 Hz, C−F), 175.8 (C); ESI-MS (m/z) 316 $(M + H)^+$; HRMS (ESI) calculated for $C_{21}H_{15}FNO$ $(M + H)^+$ 316.1138, found 316.1130.

*3-(3-Fluorophenyl)-2-(4-fluorophenyl)quinolin-4(1H)-one (**3v**).* White solid (246 mg, 74%): mp 350−352 °C; FT-IR (KBr, cm^{-1}) 3409, 3021, 1613; ^1H NMR (400 MHz, DMSO-d_6) δ 6.82 (d, J = 7.64 Hz, 1H), 6.93−6.98 (m, 2H), 7.16−7.24 (m, 3H), 7.35−7.43 (m, 3H), 7.68−7.69 (m, 2H), 8.16 (d, J = 7.96 Hz, 1H), 11.88 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 113.5 (d, J = 20.46 Hz, CH), 115.7 (d, J = 21.54 Hz, 2 × CH), 118.92 (CH), 118.98 (d, J = 20.79 Hz, CH), 119.8 (C), 123.9 (CH), 125.1 (C), 125.8 (CH), 128.3 (C), 129.5 (d, J = 8.37 Hz, CH), 131.8 (d, J = 3.38 Hz, C), 132.3 (CH), 132.4 (3 × CH), 138.7 (d, J = 8.47 Hz, C), 140.1 (C), 148.3 (C), 163.2 (d, J = 240.50 Hz, C−F), 164.0 (d, J = 245.45 Hz, C−F), 175.5 (C); ESI-MS (m/z) 334 $(M + H)^+$; HRMS (ESI) calculated for $C_{21}H_{14}F_2NO$ $(M + H)^+$ 334.1043, found 334.1047.

*3-(4-Fluorophenyl)-2-(p-tolyl)quinolin-4(1H)-one (**3w**).* White solid (217 mg, 66%): mp >385 °C; FT-IR (KBr, cm^{-1}) 3416, 3019, 1637; ^{1}HNMR (400 MHz, DMSO-d_6) δ 2.30 (s, 3H), 7.01 (t, J = 8.84 Hz, 2H), 7.07−7.11 (m, 2H), 7.16 (m, 4H), 7.34−7.38 (m, 1H), 7.66−7.71 (m, 2H), 8.15 (d, J = 7.92 Hz, 1H), 11.75 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.3 (CH_3), 114.7 (d, J = 3.38 Hz, 2 × CH) 118.9 (CH), 119.7 (C), 123.7 (CH), 125.0 (C), 125.8 (CH), 129.2 (2 × CH), 129.9 (2 × CH), 132.2 (CH), 132.6 (d, J = 3.15 Hz, C), 132.7 (C), 134.0 (d, J = 7.88 Hz, 2 × CH), 139.1 (C), 140.1 (C), 149.1 (C), 162.2 (d, J = 241.06 Hz, C−F), 175.8 (C); ESI-MS (m/z) 330 $(M + H)^+$; HRMS (ESI) calculated for $C_{22}H_{17}FNO$ $(M + H)^+$ 330.1294, found 330.1301.

*3-Phenylquinolin-4(1H)-one (**3x**).*[23] White solid (150 mg, 68%): mp 255−257 °C; FT-IR (KBr, cm^{-1}) 3408, 3019, 1638; ^1H NMR (400 MHz, DMSO-d_6) δ 7.25−7.29 (m, 1H), 7.33−7.41 (m, 3H), 7.58−7.60 (m, 1H), 7.64−7.68 (m, 1H), 7.72−7.74 (m, 2H), 8.15 (s, 1H), 8.21−8.23 (dd, J = 8.12, 1.00 Hz, 1H), 12.04 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 118.7 (CH), 120.2 (C), 123.7 (CH), 126.1 (CH), 126.3 (C), 126.8 (CH), 128.3 (2 × CH), 128.9 (2 × CH), 132.0 (CH), 136.6 (C), 138.6 (CH), 139.8 (C), 175.2 (C), ESI-MS (m/z) 222 $(M + H)^+$; HRMS (ESI) calculated for $C_{15}H_{12}NO$ $(M + H)^+$ 222.0919, found 222.0912.

*3-(3,4-Dichlorophenyl)quinolin-4(1H)-one (**3y**).* White solid (215 mg, 74%): mp 335−337 °C; FT-IR (KBr, cm^{-1}) 3401, 3019, 1633; ^1H NMR (400 MHz, DMSO-d_6) δ 7.36−7.39 (m, 1H), 7.60−7.64 (m, 2H), 7.66−7.71 (m, 1H), 7.77−7.80 (dd, J = 8.44, 2.08 Hz, 1H), 8.14 (d, J = 2.04 Hz, 1H), 8.20−8.23 (dd, J = 8.08, 1.08 Hz, 1H), 8.34 (s, 1H), 12.22 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 117.1 (C), 118.8 (CH), 124.2 (CH), 126.0 (CH), 126.3 (C), 128.6 (CH), 128.9 (C), 130.2 (CH), 130.4 (CH), 130.9 (C), 132.3 (CH), 137.3 (C), 139.4 (CH), 139.6 (C), 174.9 (C), ESI-MS (m/z) 290 $(M + H)^+$; HRMS (ESI) calculated for $C_{15}H_{10}Cl_2NO$ $(M + H)^+$ 290.0139, found 290.0139.

*7′-Chloro-2-(4-chlorophenyl)-[3,4′-biquinolin]-4(1H)-one (**3z**).* Light brown solid (217 mg, 52%): mp 348−350 °C; FT-IR (KBr, cm^{-1}) 3420, 3019, 1623; ^1H NMR (400 MHz, DMSO-d_6) δ 7.20 (d, J = 4.4 Hz, 1H), 7.29−7.34 (m, 4H), 7.40−7.7.44 (m, 1H), 7.47−7.50 (dd, J = 8.96, 2.2 Hz, 1H), 7.75−7.77 (m, 2H), 7.81 (d, J = 8.96 Hz, 1H), 8.02 (d, J = 2.12 Hz, 1H), 8.15 (d, J = 7.92 Hz, 1H), 8.75 (d, J = 4.4 Hz, 1H), 12.17 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 116.8 (C), 119.2 (CH), 124.3 (CH), 124.9 (C), 125.4 (CH), 125.7 (CH), 127.3 (CH), 128.1 (CH), 128.7 (2 × CH), 129.2 (CH), 131.1 (2 × CH), 132.8 (CH), 133.6 (C), 134.1 (C), 134.7 (C), 140.4 (C), 144.2 (C), 148.5 (C), 149.0 (C), 151.6 (CH), 175.4 (C); ESI-MS (m/z) 417 $(M + H)^+$; HRMS (ESI) calculated for $C_{24}H_{14}Cl_2N_2O$ $(M + H)^+$ 417.0561, found 417.0546.

*3-(2-Bromophenyl)-2-methylquinolin-4(1H)-one (**4a**).* White solid (195 mg, 62%): mp 286−288 °C; FT-IR (KBr, cm^{-1}) 3408, 3019, 1606; ^1H NMR (400 MHz, DMSO-d_6) δ 2.09 (s, 3H), 7.24−7.32 (m, 3H), 7.41−7.45 (m, 1H), 7.55 (d, J = 8.04 Hz, 1H), 7.63−7.71 (m, 2H), 8.06−8.08 (m, 1H), 11.71 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 18.8 (CH_3), 118.2 (CH), 121.3 (C), 123.3 (CH), 124.8 (C), 125.8 (CH), 125.9 (C), 128.1 (CH), 129.5 (CH), 132.1 (CH), 132.7 (CH), 133.5 (CH), 138.1 (C), 139.9 (C), 147.3 (C), 174.7 (C); ESI-MS (m/z) 314 $(M + H)^+$; HRMS (ESI) calculated for $C_{16}H_{13}BrNO$ $(M + H)^+$ 314.0181, found 314.0194.

*3-(3,4-Dichlorophenyl)-2-methylquinolin-4(1H)-one (**4b**).* White solid (207 mg, 68%): mp 294−296 °C; FT-IR (KBr, cm^{-1}) 3400, 3019, 1635; ^1H NMR (400 MHz, DMSO-d_6) δ 2.27 (s, 3H), 7.25−7.28 (dd, J = 8.24, 2 Hz, 1H), 7.29−7.33 (m, 1H), 7.53−7.55 (m, 2H), 7.63−7.67 (m, 2H), 8.07−8.09 (dd, J = 8.08, 1.36 Hz, 1H), 11.75 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 19.3 (CH_3), 118.2 (CH), 118.9 (C), 123.5 (CH), 124.8 (C), 125.8 (CH), 129.6 (C), 130.4 (CH), 130.9 (CH), 131.9 (CH), 132.2 (CH), 133.4 (CH), 137.4 (C), 139.8 (C), 147.6 (C), 175.0 (C); ESI-MS (m/z) 304 $(M + H)^+$; HRMS (ESI) calculated for $C_{16}H_{12}Cl_2NO$ $(M + H)^+$ 304.0296, found 304.0312.

*4-(2-Methyl-4-oxo-1,4-dihydroquinolin-3-yl)benzonitrile (**4c**).* Light pink solid (182 mg, 70%): mp 383−386 °C; FT-IR (KBr, cm^{-1}) 3401, 3019, 2232, 1636; ^1H NMR (400 MHz, DMSO-d_6) δ 2.25 (s, 3H), 7.29−7.34 (m, 1H), 7.48−7.51 (m, 2H), 7.55 (d, J = 8.04 Hz, 1H), 7.64−7.68 (m, 1H), 7.84−7.86 (m, 2H), 8.08−8.09 (dd, J = 8.04, 1.24 Hz, 1H), 11.77 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 19.3 (CH_3), 109.6 (C), 118.2 (CH), 119.6 (C), 119.8 (C), 123.6 (CH), 124.8 (C), 125.8 (CH), 132.1 (2 × CH), 132.2 (CH), 132.7 (2 × CH), 139.8 (C), 142.1 (C), 147.5 (C), 174.9 (C); ESI-MS (m/z) 261 $(M + H)^+$; HRMS (ESI) calculated for $C_{17}H_{13}N_2O$ $(M + H)^+$ 261.1028, found 261.1028.

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*2-Methyl-3-phenylquinolin-4(1H)-one (**4d**).*[13c] Light yellow solid (141 mg, 60%): mp 304−306 °C; FT-IR (KBr, cm^{-1}) 3400, 3019, 1636; ^1H NMR (400 MHz, DMSO-d_6) δ 2.22 (s, 3H), 7.23−7.32 (m, 4H), 7.37−7.41 (m, 2H), 7.53 (d, J = 7.88 Hz, 1H), 7.61−7.65 (m, 1H), 8.07−8.09 (dd, J = 8.08, 1.32 Hz, 1H), 11.62 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 19.3 (CH_3), 118.1 (CH), 121.4 (C), 123.2 (CH), 124.9 (C), 125.8 (CH), 126.9 (CH), 128.2 (2 × CH), 131.5 (2 × CH), 131.9 (CH), 136.7 (C), 139.8 (C), 146.9 (C), 175.3 (C); ESI-MS (m/z) 236 $(M + H)^+$; HRMS (ESI) calculated for $C_{16}H_{14}NO$ $(M + H)^+$ 236.1075, found 236.1063.

*3-(4-Methoxyphenyl)-2-methylquinolin-4(1H)-one (**4e**).* Light yellow solid (143 mg, 54%): mp 310−312 °C; FT-IR (KBr, cm^{-1}) 3401, 3019, 1637; ^1H NMR (400 MHz, DMSO-d_6) δ 2.22 (s, 3H), 3.78 (s, 3H), 6.95 (d, J = 8.76 Hz, 2H), 7.16 (d, J = 8.76 Hz, 2H), 7.25−7.29 (m, 1H), 7.51 (d, J = 7.92 Hz, 1H), 7.59−7.64 (m, 1H), 8.06−8.08 (dd, J = 8.04, 1.28 Hz, 1H), 11.57 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 19.4 (CH_3), 55.5 (CH_3), 113.7 (2 × CH), 118.0 (CH), 120.9 (C), 123.1 (CH), 124.8 (C), 125.8 (CH), 128.7 (C), 131.8 (CH), 132.5 (2 × CH), 139.8 (C), 146.9 (C), 158.3 (C), 175.5 (C); ESI-MS (m/z) 266 $(M + H)^+$; HRMS (ESI) calculated for $C_{17}H_{16}NO_2$ $(M + H)^+$ 266.1181, found 266.1180.

*3-(4-Bromophenyl)-2-methylquinolin-4(1H)-one (**4f**).*[11h] White solid (207 mg, 66%): mp 346−347 °C; FT-IR (KBr, cm^{-1}) 3401, 3019, 1640; ^1H NMR (400 MHz, DMSO-d_6) δ 2.23 (s, 3H), 7.21−7.23 (m, 2H), 7.27−7.32 (m, 1H), 7.53−7.58 (m, 3H), 7.62−7.66 (m, 1H), 8.07−8.09 (dd, J = 8.08, 1.40 Hz, 1H), 11.68 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 19.3 (CH_3), 118.1 (CH), 120.1 (C), 120.2 (C), 123.3 (CH), 124.8 (C), 125.8 (CH), 131.2 (2 × CH), 132.1 (CH), 133.7 (2 × CH), 135.9 (C), 139.8 (C), 147.2 (C), 175.1 (C); ESI-MS (m/z) 314 $(M + H)^+$; HRMS (ESI) calculated for $C_{16}H_{13}BrNO$ $(M + H)^+$ 314.0181, found 314.0204.

*6-(4-Chlorophenyl)benzofuro[3,2-c]quinoline (**5**).* White solid (120 mg, 75%): mp 216−218 °C; FT-IR (KBr, cm^{-1}) 3019, 2923, 1619, 1215; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29−7.33 (m, 1H), 7.49−7.53 (m, 1H), 7.59−7.62 (m, 2H), 7.67−7.71 (m, 2H), 7.75−7.82 (m, 2H), 7.89−7.92 (m, 2H), 8.29 (d, J = 8.48 Hz, 1H), 8.44−8.46 (dd, J = 8.16, 0.88 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.2 (CH), 114.4 (C), 116.3 (C), 120.9 (CH), 122.2 (CH), 122.7 (C), 123.8 (CH), 126.9 (CH), 127.3 (CH), 129.1 (2 × CH), 129.9 (2 × CH), 130.5 (2 × CH), 135.6 (C), 138.4 (C), 147.1 (C), 154.6 (C), 156.1 (C), 158.5 (C); ESI-MS (m/z) 330 $(M + H)^+$; HRMS (ESI) calculated for $C_{21}H_{13}ClNO$ $(M + H)^+$ 330.0686, found 330.0697.

*2,2,6,6-Tetramethyl-1-(4-nitrophenoxy)piperidine (**6**).*[27] White solid (145 mg, 40%): ^1H NMR (400 MHz, $CDCl_3$) δ 0.99 (s, 6H), 1.25 (s, 6H), 1.43−1.48 (m, 1H), 1.56−1.66 (m, 5H), 7.26 (s, 2H), 8.14 (d, J = 9.52 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.0 (CH_2), 20.6 (2 × CH_3), 32.4 (2 × CH_3), 39.8 (2 × CH_2), 61.1 (2 × C), 114.3 (2 × CH), 125.7 (2 × CH), 141.3 (C), 168.8 (C); DART-MS (m/z) 279.2 $(M + H)^+$.

■ ASSOCIATED CONTENT

Supporting Information

^1H and ^{13}C spectra of all compounds and X-ray crystallographic data and ORTEP diagram for compound **3c**. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00739.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: pp_yadav@cdri.res.in, ppy_cdri@yahoo.co.in.

Author Contributions

§M.R. and P.C. contributed equally to this work.

Notes

The authors declare no competing financial interest.

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