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Suzuki–Miyaura cross-coupling of 2-aryl-6,8-dibromo-1,2,3,4-tetrahydroquinolin-4-ones and subsequent dehydrogenation and oxidative aromatization of the resulting 2,6,8-triaryl-1,2,3,4-tetrahydroquinolin-4-ones

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2,6,8-Triarylquinolin-4(1*H*)-ones
2,6,8-Triaryl-4-methoxyquinolines

ABSTRACT

Dichlorobis(triphenylphosphine)palladium(II)/tricyclohexylphosphine-catalyzed Suzuki–Miyaura cross-coupling of the 2-aryl-6,8-dibromo-1,2,3,4-tetrahydroquinolin-4-ones with arylboronic acids afforded the corresponding 2,6,8-triaryl-1,2,3,4-tetrahydroquinolin-4-ones, exclusively. The latter was subjected to thallium(III) *p*-tolylsulfonate (TTS) in dimethoxyethane under reflux or to molecular iodine in methanol at reflux to afford the 2,6,8-triarylquinolin-4-(1*H*)-ones and 2,6,8-triaryl-4-methoxyquinoline derivatives, respectively.

1. Introduction

With their rich biological activities and excellent pharmacological properties,[1–3] the synthesis of 2-aryl-4-quinolinone-based compounds has been the target of a great deal of research.[4] 2-Aryl-1,2,3,4-tetrahydroquinolin-4-ones bearing substituents on the fused benzo ring are readily accessible through direct one-pot acid-catalyzed condensation of substituted aniline derivatives with ethyl benzoylacetate in refluxing toluene.[5] On the other hand, the most convenient and high yielding method developed to-date for the synthesis of polysubstituted 2-arylquinolin-4(1*H*)-ones, involves the use of 2-aminoacetophenones and substituted benzoyl chlorides as starting materials.[2,6] Less traditional syntheses of 2-arylquinolin-4(1*H*)-ones, which make use of transition metals have been developed. Palladium-catalyzed carbonylation of 2-haloanilines in the presence of terminal acetylenes, for example, afforded a variety of 2-substituted quinolin-4(1*H*)-ones in high yields.[7] Although effective, the classical and carbonylation approaches are not suited for the preparation of derivatives bearing alkyl- or aryl-containing substituents on the fused benzo ring. Consequently, methods that make use of presynthesized halogenated quinolinones and transition metals continue to be developed to allow for the adequate diversity and substitution on the fused benzo ring.[8–10] An increasingly wide range of alkyl, alkenyl, alkynyl, aryl and even heteroatom substituents can be installed on haloheteroaromatic precursors by taking advantage of the ease of displacement of the halogen atom/s on the aryl or heteroaryl moiety by nucleophiles or metal catalysts to provide an avenue for further structure elaboration. A series of 8-aryl-6-chloro-1,2,3,4-tetrahydroquinolines, for example, were recently prepared through cross-coupling of 6,8-dichloro-1,2,3,4-tetrahydroquinoline with aryl- and heteroarylmagnesium bromides (3 equiv) in the presence of dichlorobis(tricyclohexylphosphine)palladium(II) $PdCl_2(PCy_3)_2$ in tetrahydrofuran (THF) at 50–70 °C.[11]

Although a wide variety of polysubstituted quinolin-4-one derivatives have been reported earlier, a thorough literature search however revealed that 6,8-diaryl-1,2,3,4-tetrahydroquinolin-4-ones remain surprisingly unexplored so far. These substituted tetrahydroquinolin-4-ones could serve as valuable precursors for the synthesis of other medicinally important compounds, such as polysubstituted quinolin-4(1*H*)-ones and 4-alkoxyquinolines, but cannot be easily prepared through the well known classical

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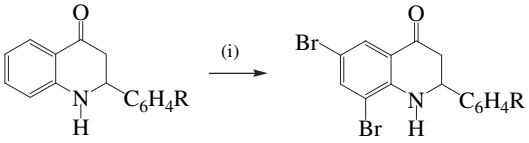
methods. With our continued interest in the palladium-catalyzed cross-coupling reactions of dihalogenoquinolines,[12] we decided to investigate the possibility of synthesizing the 2-aryl-6,8-dibromo-1,2,3,4-tetrahydroquinolin-4-ones to serve as substrates for the Suzuki–Miyaura cross-coupling with arylboronic acids. We herein describe the outcome of the Suzuki–Miyaura cross-coupling of the 2-aryl-6,8-dibromo-1,2,3,4-tetrahydroquinolin-4-ones with arylboronic acids and transformation of the resulting products through dehydrogenation and oxidative aromatization to afford polysubstituted quinolin-4(1*H*)-ones and quinoline derivatives with potential biological activity.

2. Results and discussion

The first task in this investigation was to synthesize the requisite 2-aryl-6,8-dibromo-1,2,3,4-tetrahydroquinolin-4-ones from readily available 2-aryl-1,2,3,4-tetrahydroquinolin-4-ones to serve as substrates for the palladium-catalyzed Suzuki–Miyaura cross-coupling with arylboronic acids. Whereas the *N*-tosyl-[13] and *N*-methylsulfonyl 2-aryl-2,3-dihydroquinolin-4-ones[14] are selectively brominated or iodinated at the α-carbon relative to the carbonyl group, halogenation of the 2-aryl-1,2,3,4-tetrahydroquinolin-4-ones or 1,2,3,4-tetrahydroquinoline is rather complex and depends on the conditions used.[15,16] Bromination of 2-phenyl-1,2,3,4-tetrahydroquinolin-4-one with 1 equiv of bromine in chloroform at room temperature previously afforded the 6-bromo derivative in 30% yield.[13] 2-Phenyl-1,2,3,4-tetrahydroquinolin-4-one with excess bromine (4 equiv) in chloroform, on the other hand, afforded a mixture of three products characterized as 3,6,8-tribromo-2-phenylquinolin-4(1*H*)-one, 6,8-dibromo-2-phenylquinolin-4(1*H*)-one and 6,8-dibromo-4-ethoxy-2-phenylquinoline.[15] Formation of the latter was attributed to the participation of ethanol present as a stabilizer in chloroform because the product was not detected or isolated when alcohol-free chloroform was used as solvent. Although no experimental details or analytical data of the corresponding products were provided, 2-phenyl-1,2,3,4-tetrahydroquinolin-4-one with one or 2 equiv of *N*-bromosuccinimide (NBS) in carbon tetrachloride at room temperature is reported to afford the 6-bromo- or 6,8-dibromoquinolone derivatives, respectively.[13] To establish the generality of this observation, we subjected compounds **1** to NBS (2–2.5 equiv) in carbon tetrachloride at room temperature and we isolated the corresponding 2-aryl-6,8-dibromo-2,3-dihydroquinolin-4(1*H*)-ones **2** by column chromatography on silica gel (Scheme 1).



1a-d **2a-d**

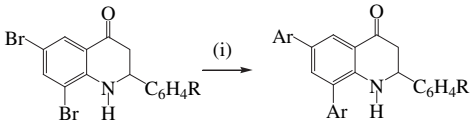
	4-R	% Yield
2a	4-H	70
2b	4-F	75
2c	4-Cl	68
2d	4-OMe	63

Reagents: (i) NBS (2.5 equiv.), CCl_4-$CHCl_3$ (3:2, v/v), rt, 3 h

Scheme 1. Bromination of 2-aryl-1,2,3,4-tetrahydroquinol-4-ones with NBS.

Bromination of **1d**, however, afforded product **2d** in relatively low yield (45%) along with an inseparable mixture of by-products presumably resulting from possible halogenation of the 2-(4-methoxyphenyl) substituent. Product **2d** was isolated in 63% yield when a mixture of carbon tetrachloride/chloroform (3:2, v/v) was used as solvent. This solvent mixture was also found to work well for substrates **1a–c** and to afford comparable yields to those obtained using CCl_4 as solvent. Products **2** are easily distinguished from the corresponding precursors by two sets of doublets at δ ca. 7.71 ppm and δ ca. 7.94 ppm corresponding to 7-H and 5-H, respectively.

Having developed a reliable method for the synthesis of dibromo-2,3-dihydroquinolin-4-ones **2**, we next focused our attention on their reactivity in Pd-catalyzed Suzuki–Miyaura cross-coupling reactions with arylboronic acids. Attempted Suzuki–Miyaura cross-coupling of **1** with a mixture of phenylboronic acid (1.0 or 2.5 equiv) and 2M K_2CO_3 in DMF in the presence of tetrakis(triphenylphosphine)palladium(0) ($Pd(PPh_3)_4$) led to the recovery of the starting material after 48 h. The failure of $Pd(PPh_3)_4$ to promote the cross-coupling is probably due to the inhibiting role of the extra PPh_3 generated in the second equilibrium {$SPd(0)(PPh_3)_3 \rightleftharpoons SPd(0)(PPh_3)_2 + PPh_3$ (K_2/[PPh_3]<<1); *S*=solvent} to afford the reactive low ligated 14-electron species ($Pd(0)(PPh_3)_2$).[17] Conversely, the oxidative addition performed by the palladium(0) complex ($Pd(0)(PPh_3)_2Cl^-$) generated by the reduction of dichlorobis(triphenylphosphine)palladium(II) ($PdCl_2(PPh_3)_2$) is reported to be more than 30 times faster than that performed from $Pd(0)(PPh_3)_4$.[17] Likewise, alkylphosphine ligands are known to coordinate with palladium and increase its electron density more than arylphosphines and, in turn, accelerate the oxidative addition and reductive elimination steps in the catalytic cycle.[18] Based on this postulate, we subjected **2a** to phenylboronic acid (1 equiv) in the presence of $PdCl_2(PPh_3)_2$/tricyclohexylphosphine (PCy_3) catalyst mixture and potassium carbonate as a base in dioxane-water (3:1, v/v) at 80–90 °C. We isolated by column chromatography on silica gel 2,6,8-triphenyl-2,3-dihydroquinolin-4(1*H*)-one **3a** (40%) along with a significant amount of the starting material due to incomplete conversion. Product **3a** was isolated in relatively high yield and as sole product with no traces of the isomeric monosubstituted derivatives or precursor when an excess of phenylboronic acid (2.5 equiv) was used (Scheme 2). The reaction conditions were



2a-d **3a-h**

	4-R	Ar	% Yield
3a	4-H	-C_6H_5	72
3b	4-F	-C_6H_5	61
3c	4-Cl	-C_6H_5	71
3d	4-OMe	-C_6H_5	62
3e	4-H	4-FC_6H_4-	61
3f	4-F	4-FC_6H_4-	51
3g	4-Cl	4-FC_6H_4-	52
3h	4-OMe	4-FC_6H_4-	66

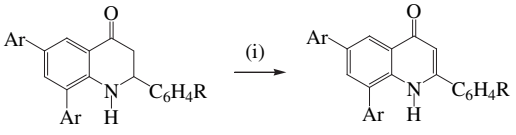
Reagents: (i) $ArB(OH)_2$ (2.5 equiv.), $PdCl_2(PPh_3)_2$, PCy_3, K_2CO_3, dioxane-water (3:1, v/v), 80–90 °C, 18 h

Scheme 2. One-pot double arylation of **2** with arylboronic acids.

extended to other substituted derivatives **2** with phenylboronic and 4-fluorophenylboronic acids to afford the corresponding 2,6,8-triarylquinolin-4-ones **3**. The observed results are complementary to the literature observation by Slugovc et al. on the $Pd(PPh_3)_4$–catalyzed Suzuki–Miyaura cross-coupling of 8-benzyloxy-5,7-dibromoquinoline with arylboronic acids to afford the 5,7-diaryl-8-benzyloxyquinolines in a single-pot operation.[19] In contrast, *m*- and *p*-dibromobenzenes were found to undergo single couplings with arylboronic acids with high selectivity whereas the *m*- and *p*-diiodobenzenes with arylboronic acids or esters led to selective double coupling reactions.[20] Lack of selectivity was also observed for the Suzuki–Miyaura cross-coupling of dihaloarenes bearing *ortho* directing groups, such as OH, NH_2, CH_2OH or NHBoc.[11]

With tetrahydroquinolin-4-ones **3** in hand, we decided to investigate the possibility of introducing a different degree of unsaturation into the heterocyclic moiety via dehydrogenation or oxidative aromatization to afford derivatives with potential antibacterial, antitumour or antimalarial activity. Although variously substituted 2-aryl-1,2,3,4-tetrahydroquinolin-4-ones have been prepared before,[4] only limited examples of their transformation into the corresponding 2-arylquinolin-4-(1*H*)-one derivatives have been reported.[21,22] One approach makes use of iodobenzene diacetate under basic conditions in methanol,[21] and the other employs thallium(III) *p*-tolylsulfonate in dimethoxyethane to afford the 2-arylquinolin-4-(1*H*)-ones.[22] We opted for the use of the readily prepared and easy-to-handle thallium(III) *p*-tolylsulfonate (TTS) in dimethoxyethane (DME), and subjected compounds **3** to dehydrogenation to afford the corresponding potentially tautomeric 2,6,8-triarylquinolin-4(1*H*)-ones **4** (Scheme 3). Their NH-4-oxo nature is confirmed by the $^{13}C{=}O$ signal at δ ca. 179.0 ppm in $CDCl_3$ and the C=O and N–H absorption bands in their IR spectra, which compare favourably with previously reported IR data for 2,8-diphenylquinolin-4(1*H*)-one.[23] The analogous 8-substituted 2-morpholin-4-yl-quinolin-4(1*H*)-ones with aryl and heteroaryl groups as the substituents have been synthesized via Suzuki–Miyaura cross-coupling of 8-bromo-2-morpholin-4-yl-1*H*-quinolin-4-one with arylboronic acids and were found to inhibit DNA-dependent protein kinase.[24]

The potentially tautomeric 2-arylquinolin-4(1*H*)-one framework has been found to undergo deprotonation by base followed by quenching with the corresponding primary alkyl halide to afford either the *O*-alkylquinoline or *N*-alkylquinolinone derivatives.[4] This classical approach however usually leads to mixtures of the *N*-alkylquinolinones and *O*-alkylquinoline isomers particularly when iodomethane is used as alkylating reagent.[3] An indirect, but sure-fire approach to the isomeric *O*-methoxyquinolines, on the other hand, involves phosphoryl chloride-promoted aromatization of the quinolin-4(1*H*)-ones and subsequent dechloromethoxylation of the resultant 4-chloroquinoline derivatives.[4] The most convenient direct synthesis of the 4-methoxy-2-arylquinoline derivatives developed to-date involves oxidative aromatization of the corresponding 2-aryl-1,2,3,4-tetrahydroquinolin-4-one precursors using oxidative reagents, such as thallium(III) nitrate[25a] or [hydroxyl(tosyloxy)iodo]benzene[25b] in trimethyl orthoformate in the presence of perchloric acid as catalyst, molecular iodine in methanol[25c] or $FeCl_3 \cdot 6H_2O$ in methanol.[25d] With an intent to synthesize the 2,6,8-triaryl-4-methoxyquinolines, we opted for the use of an iodine/alcohol mixture and subjected system **3** to molecular iodine (2 equiv) in methanol under reflux for 2.5 h. We isolated the corresponding novel 2,6,8-triaryl-4-methoxyquinolines **5a**–**h** in high yield and purity without the need for column chromatographic separation (Scheme 4). The analogous 4-alkoxy-3,6-diarylquinolines are reported to exhibit potent and selective agonism of the somatostatin receptor subtype 2 (sst_2) and to represent promising agents for the treatment of diabetic retinopathy and proliferative diseases.[26] The 6- or 8-aryl substituted 2,4-dimethoxyquinolines, on the other hand, were found to exhibit high activity against the agriculturally important nematode, *Haemonchus contortus* with potency comparable to that of the commercially available levamisole.[27] Likewise, the analogous 5,7-diaryl-8-(benzyloxy/hydroxy)quinolines show promising photoluminescence quantum yields both in the parent and the protonated states, making them suitable candidates for the active component in pH sensing applications.[20]

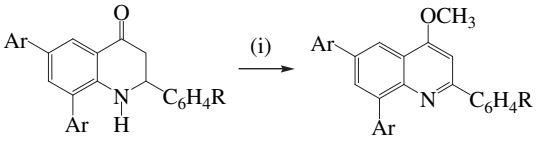


3a-h **4a-h**

	4-R	Ar	% Yield
4a	4-H	$-C_6H_5$	66
4b	4-F	$-C_6H_5$	60
4c	4-Cl	$-C_6H_5$	55
4d	4-OMe	$-C_6H_5$	55
4e	4-H	$4\text{-}FC_6H_4-$	90
4f	4-F	$4\text{-}FC_6H_4-$	50
4g	4-Cl	$4\text{-}FC_6H_4-$	71
4h	4-OMe	$4\text{-}FC_6H_4-$	65

Reagents: (i) TTS, DME, 100 °C, 30 minutes

Scheme 3. Dehydrogenation of **3** with thallium(III) *p*-tolysulfonate in dimethoxyethane.



3a-h **5a-h**

	4-R	Ar	% Yield
5a	4-H	$-C_6H_5$	82
5b	4-F	$-C_6H_5$	78
5c	4-Cl	$-C_6H_5$	97
5d	4-OMe	$-C_6H_5$	88
5e	4-H	$4\text{-}FC_6H_4-$	89
5f	4-F	$4\text{-}FC_6H_4-$	68
5g	4-Cl	$4\text{-}FC_6H_4-$	88
5h	4-OMe	$4\text{-}FC_6H_4-$	76

Reagents: (i) I_2, MeOH, 80 °C, 2 h

Scheme 4. Iodine/methanol-mediated oxidative aromatization of **3**.

The generality and brevity of iodine/methanol-mediated oxidative aromatization reaction and the accompanying yields make this methodology a suitable alternative to sequential dehydrogenation, phosphoryl chloride-promoted aromatization and dechloromethoxylation to afford methoxyquinoline derivatives.

3. Conclusions

In summary, we have demonstrated that Suzuki–Miyaura cross-coupling of 2-aryl-6,8-dibromo-1,2,3,4-tetrahydroquinolin-4-ones with arylboronic acids occurs without selectivity to afford the corresponding 2,6,8-triaryl-2,3-dihydroquinolin-4(1*H*)-ones in a single-pot operation. The heterocyclic moiety of the prepared 2,3-dihydroquinolin-4(1*H*)-ones enabled the introduction of a different degree of unsaturation in the heterocyclic framework via dehydrogenation and oxidative aromatization to afford the corresponding NH-4-oxo and 4-methoxyquinoline derivatives with potential biological activity. Moreover, the α,β-unsaturated framework of the NH-4-oxo derivatives contain several reactive centres for possible functionalization including aromatization with $POCl_3$ followed by substitution with heteroatom-containing nucleophiles or cross-coupling to afford novel polysubstituted quinolines, or C-3 halogenation and subsequent cross-coupling to afford polysubstituted 1*H*-furo[3,2-*c*]quinoline derivatives. Studies are currently underway in our laboratory to investigate the reactivity, biological and photophysical properties of the synthesized polysubstituted quinolones and quinoline derivatives.

4. Experimental

4.1. General

Melting points were recorded on a Thermocouple digital melting point apparatus and are uncorrected. IR spectra were recorded as powders using an FTS 7000 Series Digilab Win-IR Pro ATR (attenuated total reflectance) spectrometer. For column chromatography, Merck kieselgel 60 (0.063–0.200 mm) was used as stationary phase. NMR spectra were obtained as $CDCl_3$ solutions using a Varian Mercury 300 MHz NMR spectrometer and the chemical shifts are quoted relative to the solvent peaks. Low- and high-resolution mass spectra were recorded at an ionization potential of 70eV using a Micromass Autospec-TOF (double focusing high-resolution) instrument. The synthesis and characterization of substrates **1** have been described elsewhere.[28] Thallium(III) tolylsulfonate (TTS) was prepared from thallium(III) nitrate trihydrate and *p*-toluenesulfonic acid following a literature procedure.[22]

4.2. Bromination of 1 with *N*-bromosuccinimide (NBS). Typical procedure

*4.2.1. 6,8-Dibromo-2-phenyl-2,3-dihydroquinolin-4(1H)-one **2a**.* NBS (1.00 g, 5.61 mmol) was added to a stirred suspension of **1a** (0.50 g, 2.24 mmol) in carbon tetrachloride-chloroform (3:2, v/v; 40 mL). The mixture was stirred at room temperature for 3 h and then quenched with an ice-cold saturated solution of $NaHCO_3$. The organic layer was separated and the aqueous phase was extracted twice with chloroform. The combined organic phases were washed with water and dried over $MgSO_4$. The salt was filtered off and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel to afford **2a** as a yellow solid (0.86 g, 70%), mp 131–133 °C (ethanol); R_f (toluene) 0.58; ν_{max} (neat) 757, 882, 1155, 1226, 1482, 1590, 1679, 3375 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.80 (ddd, *J* 1.2, 4.5 and 16.5 Hz, 1H), 2.90 (dd, *J* 13.2 and 16.5 Hz, 1H), 4.77 (dd, *J* 4.5 and 13.2 Hz, 1H), 5.10 (br s, 1H), 7.35–7.46 (m, 5H), 7.71 (d, *J* 2.1 Hz, 1H), 7.95 (d, *J* 2.1 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 45.3, 57.7, 109.8, 110.8, 120.8, 126.5, 128.8, 129.2, 129.6, 139.9, 140.0, 147.2, 191.2; *m*/*z* (100, MH^+) 380; HRMS (ES): MH^+, found 379.9219. $C_{15}H_{12}NO^{79}Br_2^+$ requires 379.9286.

*4.2.2. 6,8-Dibromo-2-(4-fluorophenyl)-2,3-dihydroquinolin-4(1H)-one **2b**.* Yield (0.56 g, 75%), mp 126–129 °C (ethanol); R_f (toluene) 0.58; ν_{max} (neat) 833, 1160, 1225, 1480, 1592, 1684, 3363 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.78 (dd, *J* 4.5 and 16.8 Hz, 1H), 2.86 (dd, *J* 13.2 and 16.8 Hz, 1H), 4.76 (dd, *J* 4.5 and 13.2 Hz, 1H), 5.04 (br s, 1H), 7.12 (t, *J* 8.4 Hz, 2H), 7.43 (t, *J* 8.4 Hz, 2H), 7.71 (d, *J* 2.1 Hz, 1H), 7.94 (d, *J* 2.1 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 45.4, 67.1, 110.0, 110.8, 116.1 (d, $^2J_{CF}$ 21.6 Hz), 120.8, 128.3 (d, $^3J_{CF}$ 8.0 Hz), 129.6, 135.7 (d, $^4J_{CF}$ 3.2 Hz), 139.9, 147.1, 162.8 (d, $^1J_{CF}$ 246.5 Hz), 190.9; *m*/*z* (100, MH^+) 398; HRMS (ES): MH^+, found 397.9191. $C_{15}H_{11}FNO^{79}Br_2^+$ requires 397.9200.

*4.2.3. 6,8-Dibromo-2-(4-chlorophenyl)-2,3-dihydroquinolin-4-one **2c**.* Yield (0.72 g, 68%), mp 145–147 °C (ethanol); R_f (toluene) 0.63; ν_{max} (neat) 824, 1089, 1280, 1483, 1592, 1672, 3375 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.78 (dd, *J* 4.2 and 16.5 Hz, 1H), 2.85 (dd, *J* 13.2 and 16.5 Hz, 1H), 4.75 (dd, *J* 4.2 and 13.2 Hz, 1H), 5.05 (br s, 1H), 7.38 (s, 4H), 7.72 (d, *J* 2.4 Hz, 1H), 7.94 (d, *J* 2.4 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 45.2, 57.1, 110.1, 110.8, 120.7, 127.9, 129.4, 129.6, 134.6, 138.4, 139.9, 147.0, 190.8; *m*/*z* (100, MH^+) 414; HRMS (ES): MH^+, found 413.8835. $C_{15}H_{11}NO^{35}Cl^{79}Br_2^+$ requires 413.8896.

*4.2.4. 6,8-Dibromo-2-(4-methoxyphenyl)- 2,3-dihydroquinolin-4(1H)-one **2d**.* Yield (0.66 g, 63%), mp 149–151 °C (ethanol); R_f (toluene) 0.40; ν_{max} (neat) 1026, 1180, 1246, 1503, 1596, 1661, 3317 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.77 (dd, *J* 4.2 and 16.5 Hz, 1H), 2.88 (dd, *J* 13.2 and 16.5 Hz, 1H), 3.82 (s, 3H), 4.71 (dd, *J* 4.2 and 13.2 Hz, 1H), 5.03 (br s, 1H), 6.94 (d, *J* 8.7 Hz, 2H), 7.36 (d, *J* 8.7 Hz, 2H), 7.70 (d, *J* 2.1 Hz, 1H), 7.95 (d, *J* 2.1 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 45.4, 55.4, 57.2, 109.7, 110.7, 114.5, 120.8, 127.8, 129.6, 131.9, 139.8, 147.3, 159.9, 191.4; *m*/*z* (100, MH^+) 410; HRMS (ES): MH^+, found 409.9383. $C_{16}H_{14}NO_2^{79}Br_2^+$ requires 409.9391.

4.3. One-pot Suzuki cross-coupling of 2 to afford 3. Typical procedure

*4.3.1. 2,6,8-Triphenyl-2,3-dihydroquinolin-4(1H)-one **3a**.* A mixture of **2a** (0.40 g, 1.05 mmol), phenylboronic acid (0.32 g, 2.62 mmol), $PdCl_2(PPh_3)_2$ (0.04 g, 0.05 mmol), PCy_3 (0.03 g, 0.10 mmol) and K_2CO_3 (0.32 g, 2.31 mmol) in dioxane/water (3:1, v/v, 20 mL) in a two-necked flask equipped with a stirrer bar, rubber septum and a condenser was flushed for 20 min with argon gas. A balloon filled with argon gas was then connected to the top of the condenser and the mixture was heated with stirring at 80–90 °C under argon atmosphere for 18 h. The mixture was allowed to cool to room temperature and then poured into an ice-cold water. The product was taken-up into chloroform and the combined organic extracts were sequentially washed with brine, dried over anhydrous $MgSO_4$, filtered and then evaporated under reduced pressure. The residue was purified by column chromatography on silica gel to afford **3a** as a solid (0.62 g, 79%), mp 164–166 °C (ethanol); R_f (30% ethyl acetate/hexane) 0.75; ν_{max} (neat) 1234, 1474, 1675, 3380 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.84 (ddd, *J* 1.5, 4.5 and 16.3 Hz, 1H), 2.95 (dd, *J* 13.1 and 16.3 Hz, 1H), 4.70 (dd, *J* 4.5 and 13.1 Hz, 1H), 4.84 (br s, 1H), 7.27–7.52 (m, 13H), 7.60–7.63 (m, 3H), 8.20 (d, *J* 2.8 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 46.5, 58.3, 119.4, 125.0, 126.4 (2× C), 126.9, 128.1, 128.3, 128.8, 129.0, 129.1, 129.3, 129.5, 130.9, 134.8, 137.5, 139.9, 141.0, 147.9, 193.3; *m*/*z* (100, MH^+) 376; HRMS (ES): MH^+, found 376.1685. $C_{27}H_{22}NO^+$ requires 376.1701.

*4.3.2. 2-(4-Fluorophenyl)-6,8-diphenyl-2,3-dihydroquinolin-4(1H)-one **3b**.* Yield (0.24 g, 62%), mp 182–185 °C (ethanol); R_f (30% ethyl acetate/hexane) 0.75; ν_{max} (neat) 1232, 1481, 1600, 1681,

3381 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.82 (ddd, *J* 1.5, 4.5 and 16.3 Hz, 1H), 2.92 (dd, *J* 12.9 and 16.3 Hz, 1H), 4.70 (dd, *J* 4.5 and 12.9 Hz, 1H), 4.78 (br s, 1H), 7.05 (t, *J* 8.7 Hz, 2H), 7.27–7.51 (m, 10H), 7.59–7.62 (m, 3H), 8.19 (d, *J* 1.8 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 46.5, 57.6, 115.9 (d, $^2J_{CF}$ 21.4 Hz), 119.5, 125.0, 126.4, 126.9, 128.0, 128.1 (d, $^3J_{CF}$ 8.3 Hz), 128.2, 128.8, 129.1, 129.3, 129.5, 131.2, 134.9, 136.8 (d, $^4J_{CF}$ 3.2 Hz), 137.4, 139.8, 147.8 (d, $^1J_{CF}$ 245.9 Hz), 193.1; *m*/*z* (100, MH^+) 394; HRMS (ES): MH^+, found 394.1599. $C_{27}H_{21}FNO^+$ requires 394.1607.

4.3.3. 2-(4-Chlorophenyl)-6,8-diphenyl-2,3-dihydroquinolin-4(1H)-one ***3c***. Yield (0.28 g, 72%), mp 202–204 °C (ethanol); R_f (30% ethyl acetate/hexane) 0.75; ν_{max} (neat) 1274, 1479, 1666, 3373 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.87 (dd, *J* 4.5 and 16.2 Hz, 1H), 2.91 (dd, *J* 12.3 and 16.2 Hz, 1H), 4.70 (dd, *J* 4.5 and 12.3 Hz, 1H), 4.77 (br s, 1H), 7.33 (s, 4H), 7.37–7.50 (m, 8H), 7.59–7.62 (m, 3H), 8.18 (d, *J* 2.7 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 46.3, 57.6, 119.5, 125.0, 126.4, 126.9, 127.6, 128.2, 128.8, 129.1, 129.2, 129.3, 129.6, 131.2, 134.1, 134.9, 137.4, 139.5, 139.8, 147.7, 192.9; *m*/*z* (100, MH^+) 410; HRMS (ES): MH^+, found 410.1300. $C_{27}H_{21}NO^{35}Cl^+$ requires 410.1312.

4.3.4. 2-(4-Methoxyphenyl)-6,8-diphenyl-2,3-dihydroquinolin-4(1H)-one ***3d***. Yield (0.24 g, 62%), mp 194–196 °C (ethanol); R_f (30% ethyl acetate/hexane) 0.62; ν_{max} (neat) 1240, 1478, 1607, 1675, 3400 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.80 (ddd, *J* 1.5, 3.9 and 16.2 Hz, 1H), 2.93 (dd, *J* 13.2 and 16.2 Hz, 1H), 3.79 (s, 3H), 4.66 (dd, *J* 3.9 and 13.2 Hz, 1H), 4.78 (br s, 1H), 6.89 (d, *J* 8.7 Hz, 2H), 7.31 (d, *J* 8.7 Hz, 2H), 7.36–7.51 (m, 8H), 7.58–7.63 (m, 3H), 8.19 (d, *J* 2.4 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 46.6, 55.3, 57.7, 114.3, 119.4, 125.0, 126.3, 126.8, 127.6, 128.1, 128.8, 129.1, 129.2, 129.5, 130.8, 133.0, 134.8, 137.5, 139.9, 148.0, 159.5, 193.5; *m*/*z* (100, MH^+) 406; HRMS (ES): MH^+, found 406.1790. $C_{28}H_{24}NO_2^+$ requires 406.1807.

4.3.5. 6,8-Bis(4-fluorophenyl)-2-phenyl-2,3-dihydroquinolin-4(1H)-one ***3e***. Yield (0.28 g, 66%), mp 167–169 °C (ethanol); R_f (30% ethyl acetate/hexane) 0.71; ν_{max} (neat) 835, 1218, 1490, 1603, 1682, 3390 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.84 (ddd, *J* 1.5, 4.5 and 16.2 Hz, 1H), 2.94 (dd, *J* 12.9 and 16.2 Hz, 1H), 4.70 (br s, 1H), 4.71 (dd, *J* 4.5 and 12.9 Hz, 1H), 7.10 (t, *J* 8.7 Hz, 2H), 7.16 (t, *J* 8.7 Hz, 2H), 7.31–7.43 (m, 5H), 7.42–7.57 (m, 5H), 8.13 (d, *J* 2.4 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 46.4, 58.2, 115.6 (d, $^2J_{CF}$ 21.4 Hz), 115.8 (d, $^2J_{CF}$ 21.4 Hz), 119.5, 125.0, 126.3, 127.9 (d, $^3J_{CF}$ 8.0 Hz), 128.4, 128.6, 129.1, 130.1, 130.8 (d, $^3J_{CF}$ 8.0 Hz), 133.2 (d, $^3J_{CF}$ 3.4 Hz), 134.6, 135.9 (d, $^4J_{CF}$ 3.1 Hz), 140.8, 147.9, 162.2 (d, $^1J_{CF}$ 244.5 Hz), 162.5 (d, $^1J_{CF}$ 246.7 Hz), 193.1; *m*/*z* (100, MH^+) 412; HRMS (ES): MH^+, found 412.1492. $C_{27}H_{20}F_2NO^+$ requires 412.1513.

4.3.6. 2,6,8-Tris(4-fluorophenyl)-2,3-dihydroquinolin-4(1H)-one ***3f***. Yield (0.44 g, 51%), mp 176–179 °C (ethanol); R_f (30% ethyl acetate/hexane) 0.70; ν_{max} (neat) 835, 1218, 1490, 1603, 1682, 3390 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.81 (ddd, *J* 1.5, 4.5 and 16.2 Hz, 1H), 2.91 (dd, *J* 12.9 and 16.2 Hz, 1H), 4.67 (br s, 1H), 4.70 (dd, *J* 4.5 and 12.9 Hz, 1H), 7.02–7.13 (m, 4H), 7.16 (t, *J* 7.8 Hz, 2H), 7.37 (t, *J* 6.9 Hz, 2H), 7.54 (t, *J* 6.9 Hz, 2H), 7.50 (d, *J* 2.1 Hz, 1H), 7.57 (t, *J* 6.9 Hz, 2H), 8.13 (d, *J* 2.4 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 46.4, 57.6, 115.7 (d, $^2J_{CF}$ 21.4 Hz), 116.0 (d, $^2J_{CF}$ 21.6 Hz), 116.3 (d, $^2J_{CF}$ 21.4 Hz), 119.5, 125.0, 127.8 (d, $^3J_{CF}$ 8.0 Hz), 127.9 (d, $^3J_{CF}$ 8.3 Hz), 128.0, 128.6, 130.2, 130.8 (d, $^3J_{CF}$ 8.0 Hz), 133.1 (d, $^4J_{CF}$ 3.5 Hz), 134.7, 135.8 (d, $^4J_{CF}$ 3.2 Hz), 136.6 (d, $^4J_{CF}$ 3.5 Hz), 147.7, 162.2 (d, $^1J_{CF}$ 244.4 Hz), 162.5 (d, $^1J_{CF}$ 245.0 Hz, 2× C), 193.0; *m*/*z* (100, MH^+) 430; HRMS (ES): MH^+, found 430.1421. $C_{27}H_{19}F_3NO^+$ requires 430.1419.

4.3.7. 2-(4-Chlorophenyl)-6,8-bis(4-fluorophenyl)-2,3-dihydroquinolin-4(1H)-one ***3g***. Yield (0.23 g, 52%), mp 190–192 °C (ethanol); R_f (30% ethyl acetate/hexane) 0.71; ν_{max} (neat) 834, 1014, 1231, 1487, 1678, 3392 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.62 (dd, *J* 4.8 and 16.3 Hz, 1H), 2.90 (dd, *J* 12.6 and 16.3 Hz, 1H), 4.64 (br s, 1H), 4.69 (dd, *J* 4.8 and 12.6 Hz, 1H), 7.09 (t, *J* 8.4 Hz, 2H), 7.16 (t, *J* 8.4 Hz, 2H), 7.33 (s, 4H), 7.45 (t, *J* 6.9 Hz, 2H), 7.51 (d, *J* 2.1 Hz, 1H), 7.54 (t, *J* 6.9 Hz, 2H), 8.20 (d, *J* 2.8 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 46.2, 57.6, 115.7 (d, $^2J_{CF}$ 21.3 Hz), 116.4 (d, $^2J_{CF}$ 21.3 Hz), 119.5, 125.0, 127.7, 127.9 (d, $^3J_{CF}$ 8.0 Hz), 128.6, 129.3, 130.4, 130.8 (d, $^3J_{CF}$ 8.0 Hz), 133.1 (d, $^4J_{CF}$ 3.3 Hz), 134.2, 134.7, 135.8 (d, $^4J_{CF}$ 3.2 Hz), 139.3, 147.6, 162.2 (d, $^1J_{CF}$ 244.7 Hz), 162.5 (d, $^1J_{CF}$ 246.9 Hz), 192.7; *m*/*z* (100, MH^+) 446; HRMS (ES): MH^+, found 446.1101. $C_{27}H_{19}F_2NO^{35}Cl^+$ requires 446.1123.

4.3.8. 6,8-Bis(4-fluorophenyl)-2-(4-methoxyphenyl)-2,3-dihydroquinolin-4(1H)-one ***3h***. Yield (0.28 g, 66%), mp 182–184 °C (ethanol); R_f (30% ethyl acetate/hexane) 0.64; ν_{max} (neat) 830, 1220, 1484, 1509, 1676, 3402 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.80 (dd, *J* 3.0 and 16.8 Hz, 1H), 2.90 (dd, *J* 12.6 and 16.8 Hz, 1H), 3.80 (s, 3H), 4.65 (br s, 1H), 4.65 (dd, *J* 4.5 and 12.6 Hz, 1H), 6.89 (d, *J* 7.5 Hz, 2H), 7.09 (t, *J* 7.8 Hz, 1H), 7.13 (d, *J* 9.0 Hz, 2H), 7.15 (t, *J* 7.8 Hz, 1H), 7.30 (d, *J* 9.0 Hz, 2H), 7.42–7.56 (m, 5H), 8.13 (d, *J* 3.0 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 46.5, 55.3, 57.7, 114.4, 115.6 (d, $^2J_{CF}$ 21.4 Hz), 116.3 (d, $^2J_{CF}$ 21.4 Hz), 119.5, 125.0, 127.6, 127.9 (d, $^3J_{CF}$ 8.0 Hz), 128.5, 130.0, 130.8 (d, $^2J_{CF}$ 8.0 Hz), 132.8, 133.2 (d, $^3J_{CF}$ 3.4 Hz), 134.6, 135.9 (d, $^4J_{CF}$ 3.3 Hz), 147.9, 159.6, 162.2 (d, $^1J_{CF}$ 244.5 Hz), 162.5 (d, $^1J_{CF}$ 246.5 Hz), 193.4; *m*/*z* (100, MH^+) 442; HRMS (ES): MH^+, found 442.1628. $C_{28}H_{22}F_2NO_2^+$ requires 442.1619.

4.4. Dehydrogenation of 3 with thallium(III) *p*-tolysulfonate (TTS). Typical procedure

4.4.1. 2,6,8-Triphenylquinolin-4(1H)-one ***4a***. A stirred mixture of **3a** (0.20 g, 0.53 mmol) and TTS (0.43 g, 0.59 mmol) in DME (10 mL) was heated at 100 °C for 30 min. The cooled reaction mixture was quenched with water and the resulting precipitate was filtered on a sintered funnel. The crude product was taken-up into chloroform and the organic solution was washed with saturated Na_2CO_3 and dried over $MgSO_4$. The salt was filtered off and the solvent was concentrated under reduced pressure to afford **4a** as a solid (0.13 g, 66%), mp 241–243 °C (ethanol); ν_{max} (neat) 695, 759, 1492, 1591, 1626, 3398 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 6.63 (d, *J* 1.8 Hz, 1H), 6.80 (d, *J* 7.8 Hz, 1H), 7.11 (d, *J* 8.1 Hz, 1H), 7.37 (t, *J* 7.2 Hz, 1H), 7.44–7.64 (m, 10H), 7.75 (d, *J* 7.2 Hz, 2H), 7.85 (d, *J* 2.1 Hz, 1H), 8.49 (br s, 1H), 8.67 (d, *J* 1.8 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 108.3, 113.9, 123.4, 126.1, 127.2, 127.6, 127.8, 128.9, 129.0, 129.2, 129.6, 129.8, 130.8, 131.8, 134.5, 136.4, 136.6, 136.5, 139.7, 148.7, 179.0; *m*/*z* (100, MH^+) 374; HRMS (ES): MH^+, found 374.1530. $C_{27}H_{20}NO^+$ requires 374.1545.

4.4.2. 2-(4-Fluorophenyl)-6,8-diphenylquinolin-4(1H)-one ***4b***. Yield (0.12 g, 60%), mp 237–238 °C (ethanol); ν_{max} (neat) 697, 770, 832, 1236, 1500, 1507, 1592, 1635, 3415 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 6.56 (d, *J* 1.8 Hz, 1H), 6.79 (d, *J* 8.4 Hz, 2H), 7.10 (d, *J* 8.4 Hz, 2H), 7.17 (t, *J* 8.7 Hz, 2H), 7.36 (t, *J* 7.2 Hz, 1H), 7.43–7.65 (m, 5H), 7.73 (d, *J* 7.2 Hz, 2H), 7.85 (d, *J* 2.1 Hz, 1H), 8.42 (br s, 1H), 8.66 (d, *J* 2.1 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 108.2, 113.9, 116.7 (d, $^2J_{CF}$ 21.9 Hz), 123.4, 125.8, 127.1, 127.6, 127.7, 128.1 (d, $^3J_{CF}$ 8.6 Hz), 128.9, 129.0, 129.1, 129.8, 130.6 (d, $^4J_{CF}$ 3.2 Hz), 131.4, 131.8, 136.2, 136.6, 139.5, 147.7, 164.1 (d, $^1J_{CF}$ 251.0 Hz), 178.9; *m*/*z* (100, MH^+) 392; HRMS (ES): MH^+, found 392.1465. $C_{27}H_{19}FNO^+$ requires 392.1451.

4.4.3. 2-(4-Chlorophenyl)-6,8-diphenylquinolin-4(1H)-one ***4c***. Yield (0.11 g, 55%), mp 209–211 °C (ethanol); ν_{max} (neat) 697, 759, 828, 1093, 1246, 1381, 1489, 1596, 1623, 3401 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 6.57 (s, 1H), 6.80 (d, *J* 7.8 Hz, 1H), 7.10 (d, *J* 9.3 Hz, 1H), 7.37 (t, *J* 7.8 Hz, 1H), 7.42–7.64 (m, 10H), 7.74 (d, *J* 7.5 Hz, 2H), 7.84 (d, *J* 2.1 Hz, 1H), 8.42 (br s, 1H), 8.65 (d, *J* 2.1 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 108.4, 113.9, 123.5, 125.8, 127.2, 127.4, 127.7, 128.9, 129.1, 129.2, 129.8, 129.9, 131.4, 131.9, 132.9, 136.1, 136.2, 136.8, 139.6, 147.5, 179.0; *m*/*z* (100,

MH^+) 408; HRMS (ES): MH^+, found 408.1148. $C_{27}H_{19}NO^{35}Cl^+$ requires 408.1147.

4.4.4. 2-(4-Methoxyphenyl)-6,8-diphenylquinolin-4(1H)-one ***4d***. Yield (0.12 g, 55%), mp 210–212 °C (ethanol); ν_{max} (neat) 701, 765, 832, 1220, 1482, 1669, 3376 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.85 (s, 3H), 6.58 (d, *J* 1.5 Hz, 1H), 6.99 (d, *J* 8.7 Hz, 2H), 7.36 (t, *J* 7.8 Hz, 1H), 7.44 (d, *J* 7.8 Hz, 2H), 7.45 (d, *J* 8.7 Hz, 2H), 7.50–7.64 (m, 5H), 7.75 (d, *J* 7.2 Hz, 2H), 7.83 (d, *J* 2.1 Hz, 1H), 8.45 (br s, 1H), 8.66 (d, *J* 2.1 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 55.5, 107.5, 115.0, 123.5, 125.9, 126.5, 127.1, 127.5, 127.6, 128.8, 128.9, 129.2, 129.8, 131.3, 131.7, 136.1, 136.3, 136.4, 139.7, 148.5, 161.6, 179.0; *m/z* (100, MH^+) 404; HRMS (ES): MH^+, found 404.1634. $C_{28}H_{22}NO_2^+$ requires 404.1651.

4.4.5. 6,8-Bis(4-fluorophenyl)-2-phenylquinolin-4(1H)-one ***4e***. Yield (0.09 g, 90%), mp 239–242 °C (ethanol); ν_{max} (neat) 834, 1218, 1495, 1584, 1628, 3405 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 6.61 (d, *J* 1.8 Hz, 1H), 7.14 (t, *J* 8.7 Hz, 2H), 7.31 (t, *J* 8.7 Hz, 2H), 7.50 (s, 5H), 7.57 (t, *J* 8.7 Hz, 2H), 7.67 (t, *J* 8.7 Hz, 2H), 7.74 (d, *J* 2.1 Hz, 1H), 8.34 (br s, 1H), 8.59 (d, *J* 2.1 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 108.4, 115.8 (d, $^2J_{CF}$ 21.4 Hz), 116.9 (d, $^2J_{CF}$ 21.6 Hz), 123.5, 125.9, 126.1, 128.7 (d, $^3J_{CF}$ 8.0 Hz), 129.7, 130.4, 130.8, 131.0 (d, $^3J_{CF}$ 8.0 Hz), 131.7, 132.1 (d, $^4J_{CF}$ 3.4 Hz), 134.3, 135.5, 135.6 (d, $^4J_{CF}$ 3.4 Hz), 136.2, 148.8, 162.7 (d, $^1J_{CF}$ 245.6 Hz), 163.0 (d, $^1J_{CF}$ 248.4 Hz), 178.8; *m/z* (100, MH^+) 410; HRMS (ES): MH^+, found 410.1343. $C_{27}H_{18}NF_2O^+$ requires 410.1356.

4.4.6. 2,6,8-Tris(4-fluorophenyl)quinolin-4(1H)-one ***4f***. Yield (0.06 g, 50%), mp 240–242 °C (ethanol); ν_{max} (neat) 832, 839, 1237, 1497, 1591, 1627, 3406 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 6.52 (s, 1H), 7.14 (t, *J* 9.0 Hz, 2H), 7.18 (t, *J* 9.0 Hz, 2H), 7.31 (t, *J* 9.0 Hz, 2H), 7.48 (t, *J* 7.5 Hz, 2H), 7.56 (t, *J* 7.5 Hz, 2H), 7.66 (t, *J* 7.5 Hz, 2H), 7.74 (d, *J* 2.4 Hz, 1H), 8.25 (br s, 1H), 8.57 (d, *J* 2.4 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 108.3, 115.8 (d, $^2J_{CF}$ 21.3 Hz), 116.84 (d, $^2J_{CF}$ 22.2 Hz), 117.0 (d, $^2J_{CF}$ 21.6 Hz), 123.4, 125.8, 128.1 (d, $^3J_{CF}$ 8.4 Hz), 128.7 (d, $^3J_{CF}$ 8.3 Hz), 130.4, 130.5 (d, $^3J_{CF}$ 3.4 Hz), 131.0 (d, $^3J_{CF}$ 8.0 Hz), 131.7, 132.1 (d, $^3J_{CF}$ 3.4 Hz), 135.6 (d, $^3J_{CF}$ 3.4 Hz), 135.7, 136.1, 147.8, 162.7 (d, $^1J_{CF}$ 246.2 Hz), 163.0 (d, $^1J_{CF}$ 261.9 Hz), 164.2 (d, $^1J_{CF}$ 251.3 Hz), 178.7; *m/z* (100, MH^+) 428; HRMS (ES): MH^+, found 428.1252. $C_{27}H_{17}NF_3O^+$ requires 428.1262.

4.4.7. 2-(4-Chlorophenyl)-6,8-bis(4-fluorophenyl)quinolin-4(1H)-one ***4g***. Yield (0.07 g, 71%), mp 225–228 °C (ethanol); ν_{max} (neat) 828, 1094, 1158, 1224, 1490, 1601, 1624 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 6.56 (d, *J* 1.8 Hz, 1H), 7.15 (t, *J* 8.7 Hz, 2H), 7.31 (t, *J* 8.7 Hz, 2H), 7.43 (d, *J* 9.0 Hz, 2H), 7.48 (d, *J* 9.0 Hz, 2H), 7.56 (t, *J* 8.7 Hz, 2H), 7.68 (t, *J* 8.7 Hz, 2H), 7.75 (d, *J* 2.1 Hz, 1H), 8.24 (br s, 1H), 8.59 (d, *J* 2.1 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 108.5, 115.9 (d, $^2J_{CF}$ 21.4 Hz), 117.0 (d, $^2J_{CF}$ 21.3 Hz), 123.5, 125.9, 127.4, 128.7 (d, $^3J_{CF}$ 8.0 Hz), 130.0, 130.4, 131.0 (d, $^3J_{CF}$ 8.3 Hz), 131.8, 132.0 (d, $^4J_{CF}$ 3.7 Hz), 132.8, 135.6 (d, $^4J_{CF}$ 3.6 Hz), 135.8, 136.1, 137.2, 147.6, 162.7 (d, $^1J_{CF}$ 245.9 Hz), 163.1 (d, $^1J_{CF}$ 248.5 Hz), 178.8; *m/z* (100, MH^+) 444; HRMS (ES): MH^+, found 444.0957. $C_{27}H_{17}F_2NO^{35}Cl^+$ requires 444.0967.

4.4.8. 6,8-Bis(4-fluorophenyl)-2-(4-methoxyphenyl)quinolin-4(1H)-one ***4h***. Yield (0.13 g, 65%), mp 219–220 °C (ethanol); ν_{max} (neat) 827, 1158, 1223, 1501, 1508, 1582, 1628, 3413 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.85 (s, 3H), 6.56 (s, 1H), 7.01 (d, *J* 9.3 Hz, 2H), 7.14 (t, *J* 9.3 Hz, 2H), 7.31 (t, *J* 9.3 Hz, 2H), 7.43 (d, *J* 9.3 Hz, 2H), 7.57 (t, *J* 7.8 Hz, 2H), 7.67 (t, *J* 7.8 Hz, 2H), 7.73 (d, *J* 1.8 Hz, 1H), 8.28 (br s, 1H), 8.58 (d, *J* 1.8 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 55.5, 107.5, 115.0, 115.9 (d, $^2J_{CF}$ 21.4 Hz), 116.9 (d, $^2J_{CF}$ 21.4 Hz), 123.5, 125.8, 126.4, 127.4, 128.7 (d, $^3J_{CF}$ 8.0 Hz), 130.3, 131.1 (d, $^3J_{CF}$ 8.3 Hz), 131.5, 132.2 (d, $^4J_{CF}$ 3.4 Hz), 135.4, 135.7 (d, $^4J_{CF}$ 3.4 Hz), 136.1, 148.5, 161.7, 162.6 (d, $^1J_{CF}$ 245.9 Hz), 163.0 (d, $^1J_{CF}$ 248.1 Hz), 178.8; *m/z* (100, MH^+) 440; HRMS (ES): MH^+, found440.1300. $C_{28}H_{20}F_2O_2N^+$ requires 440.1310.

4.5. Aromatization of 3 with iodine in methanol. Typical procedure

4.5.1. 4-Methoxy-2,6,8-triphenylquinoline ***5a***. A stirred mixture of **3a** (0.20 g, 0.27 mmol) and iodine (0.14 g, 0.53 mmol) in methanol (15 mL) was refluxed for 2.5 h. The mixture was quenched with an ice-cold solution of saturated sodium thiosulfate and the product was extracted into chloroform. The combined chloroform phases were dried over $MgSO_4$, filtered and then evaporated under reduced pressure to afford **6a** as a white solid (0.17 g, 82%), mp 220–223 °C (ethanol); ν_{max} (neat) 692, 768, 835, 1219, 1486, 1592 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 4.16 (s, 3H), 7.30 (s, 1H), 7.39–7.55 (m, 9H), 7.80 (d, *J* 7.5 Hz, 2H), 7.91 (d, *J* 7.5 Hz, 2H), 8.05 (d, *J* 1.8 Hz, 1H), 8.14 (d, *J* 8.1 Hz, 2H), 8.43 (d, *J* 1.8 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 55.7, 97.2, 119.0, 121.2, 127.1, 127.3, 127.4, 127.5, 127.6, 128.6, 128.9, 129.2, 130.4, 131.2, 137.7, 139.8, 140.0, 140.7 (2× C), 145.9, 157.1, 163.2; *m/z* (100, MH^+) 388; HRMS (ES): MH^+, found 388.1709. $C_{28}H_{22}NO^+$ requires 388.1706.

4.5.2. 2-(4-Fluorophenyl)-4-methoxy-6,8-diphenylquinoline ***5b***. Yield (0.08 g, 78%), mp 210–212 °C (ethanol); ν_{max} (neat) 699, 765, 825, 1219, 1484, 1589 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 4.16 (s, 3H), 7.13 (t, *J* 8.4 Hz, 2H), 7.23 (s, 1H), 7.36–7.55 (m, 6H), 7.79 (d, *J* 7.5 Hz, 2H), 7.87 (d, *J* 7.5 Hz, 2H), 8.04 (d, *J* 2.1 Hz, 1H), 8.12 (t, *J* 8.4 Hz, 2H), 8.42 (d, *J* 2.1 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 55.7, 96.8, 115.5(d, $^2J_{CF}$ 21.6 Hz), 118.7, 121.1, 127.2, 127.4, 127.5, 127.7, 128.9, 129.2 (d, $^3J_{CF}$ 8.3 Hz), 130.5, 131.1, 136.1 (d, $^4J_{CF}$ 3.2 Hz), 137.7, 139.8, 140.7, 145.8, 156.0, 163.3, 163.7 (d, $^1J_{CF}$ 247.3 Hz); *m/z* (100, MH^+) 406; HRMS (ES): MH^+, found 406.1606. $C_{28}H_{21}NFO^+$ requires 406.1607.

4.5.3. 2-(4-Chlorophenyl)-4-methoxy-6,8-diphenylquinoline ***5c***. Yield (0.20 g, 97%), mp 231–233 °C (ethanol); ν_{max} (neat) 698, 760, 824, 1094, 1218, 1483, 1590 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 4.14 (s, 3H), 7.22 (s, 1H), 7.40–7.55 (m, 8H), 7.79 (d, *J* 8.4 Hz, 2H), 7.87 (d, *J* 8.4 Hz, 2H), 8.06 (d, *J* 8.4 Hz, 2H), 8.07 (d, *J* 2.4 Hz, 1H), 8.41 (d, *J* 2.4 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 55.7, 96.8, 119.0, 121.2, 127.2, 127.4, 127.6, 127.7, 128.6, 128.8, 128.9, 130.5, 131.1, 135.3, 137.9, 138.4, 139.7, 140.6, 140.7, 145.8, 155.7, 163.3; *m/z* (100, MH^+) 422; HRMS (ES): MH^+, found 422.1296. $C_{28}H_{21}NO^{35}Cl^+$ requires 422.1312.

4.5.4. 4-Methoxy-2-(4-methoxyphenyl)-6,8-diphenylquinoline ***5d***. Yield (0.08 g, 87%), mp 196–198 °C (ethanol); ν_{max} (neat) 697, 758, 825, 1207, 1168, 1217, 1233, 1484, 1591 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.85 (s, 3H), 4.14 (s, 3H), 6.97 (d, *J* 9.0 Hz, 2H), 7.22 (s, 1H), 7.35–7.59 (m, 6H), 7.89 (d, *J* 7.7 Hz, 2H), 7.89 (d, *J* 8.7 Hz, 2H), 8.02 (d, *J* 2.1 Hz, 1H), 8.09 (d, *J* 8.7 Hz, 2H), 8.40 (d, *J* 2.1 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 55.3, 55.6, 96.6, 114.0, 118.9, 120.9, 127.0, 127.3, 127.4, 127.6, 128.7, 128.8, 130.3, 131.2, 132.6, 137.3, 139.9, 140.5, 140.8, 145.9, 156.7, 160.7, 163.0; *m/z* (100, MH^+) 418; HRMS (ES): MH^+, found 418.1816. $C_{29}H_{24}NO_2^+$ requires 418.1807.

4.5.5. 6,8-Bis(4-fluorophenyl)-4-methoxy-2-phenylquinoline ***5e***. Yield (0.09 g, 89%), mp 231–233 °C (ethanol); ν_{max} (neat) 772, 832, 1159, 1219, 1486, 1509, 1593 cm^{-1}; δ_H (300 MHz, $CDCl_3$); 4.17 (s, 3H), 7.17 (d, *J* 8.4 Hz, 2H), 7.22 (d, *J* 8.4 Hz, 2H), 7.30 (s, 1H), 7.39–7.51 (m, 3H), 7.74 (t, *J* 8.7 Hz, 2H), 7.85 (t, *J* 8.7 Hz, 2H), 7.93 (d, *J* 2.1 Hz, 1H), 8.12 (d, *J* 8.4 Hz, 2H), 8.36 (d, *J* 2.1 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 55.8, 97.3, 114.5 (d, ^2J 21.3 Hz), 115.8 (d, ^2J 21.4 Hz), 118.9, 121.2, 127.3, 128.7, 130.0 (d, $^3J_{CF}$ 8.0 Hz), 129.4, 130.0, 132.7 (d, $^3J_{CF}$ 8.0 Hz), 135.6 (d, $^4J_{CF}$ 3.5 Hz), 136.7, 136.8 (d, $^4J_{CF}$ 3.5 Hz), 139.7, 139.8, 145.7, 157.3, 162.4 (d, $^1J_{CF}$ 244.7 Hz), 162.6 (d, $^1J_{CF}$ 245.0 Hz), 163.1; *m/z* (100, MH^+) 424; HRMS (ES): MH^+, found 424.1519. $C_{28}H_{20}F_2NO^+$ requires 424.1513.

4.5.6. 2,6,8-Tris(4-fluorophenyl)-4-methoxyquinoline ***5f***. Yield (0.07 g, 68%), mp 197–199 °C (ethanol); ν_{max} (neat) 819, 1155, 1216, 1509, 1586 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 4.16 (s, 3H), 7.15 (t, *J* 8.7 Hz, 2H), 7.21 (t, *J* 8.7 Hz, 2H), 7.23 (t, *J* 8.7 Hz, 2H), 7.24 (s, 1H), 7.73 (t, *J* 8.7 Hz, 2H),

7.81 (t, *J* 8.7 Hz, 2H), 7.92 (d, *J* 2.1 Hz, 1H), 8.10 (t, *J* 8.7 Hz, 2H), 8.35 (d, *J* 2.1 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 55.7, 96.9, 114.6 (d, $^2J_{CF}$ 21.1 Hz), 115.6 (d, $^2J_{CF}$ 21.7 Hz), 115.8 (d, $^2J_{CF}$ 21.1 Hz), 118.9, 121.0, 128.9 (d, $^3J_{CF}$ 8.0 Hz), 129.1 (d, $^3J_{CF}$ 8.0 Hz), 130.1, 132.6 (d, $^3J_{CF}$ 8.0 Hz), 135.6 (d, $^4J_{CF}$ 3.2 Hz), 136.0 (d, $^4J_{CF}$ 3.2 Hz), 136.6 (d, $^4J_{CF}$ 3.2 Hz), 136.7, 139.7, 145.6, 156.1, 162.3 (d, $^1J_{CF}$ 244.7 Hz), 162.6 (d, $^1J_{CF}$ 245.6 Hz), 163.2, 163.7 (d, $^1J_{CF}$ 247.6 Hz); *m*/*z* (100, MH^+) 442; HRMS (ES): MH^+, found 442.1408. $C_{28}H_{19}F_3NO^+$ requires 442.1419.

4.5.7. 2-Chlorophenyl-6,8-bis(4-fluorophenyl)-4-methoxyquinoline ***5g***. Yield (0.09 g, 88%), mp 236–238 °C (ethanol); ν_{max} (neat) 819, 1094, 1156, 1212, 1234, 1480, 1512 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 4.16 (s, 3H), 7.16 (d, *J* 8.4 Hz, 2H), 7.22 (d, *J* 8.4 Hz, 2H), 7.24 (s, 1H), 7.43 (d, *J* 8.4 Hz, 2H), 7.73 (t, *J* 8.7 Hz, 2H), 7.81 (t, *J* 8.7 Hz, 2H), 7.93 (d, *J* 2.1 Hz, 1H), 8.04 (d, *J* 8.7 Hz, 2H), 8.35 (d, *J* 2.1 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 55.8, 96.9, 114.6 (d, $^2J_{CF}$ 21.1 Hz), 115.7 (d, $^2J_{CF}$ 21.1 Hz), 118.9, 121.2, 128.5, 128.8, 128.9 (d, $^3J_{CF}$ 8.3 Hz), 129.0, 130.1, 132.6 (d, $^3J_{CF}$ 8.0 Hz), 135.4 (d, $^4J_{CF}$ 2.5 Hz), 135.5, 136.7 (d, $^4J_{CF}$ 3.1 Hz), 136.9, 138.2, 139.8, 156.0, 162.4 (d, $^1J_{CF}$ 244.7 Hz), 162.7 (d, $^1J_{CF}$ 245.6 Hz), 163.3; *m*/*z* (100, MH^+) 458; HRMS (ES): MH^+, found 458.1135. $C_{28}H_{19}F_2NO^{35}Cl^+$ requires 458.1123.

4.5.8. 6,8-Bis(4-fluorophenyl)-4-methoxy-2-(4-methoxyphenyl) quinoline ***5h***. Yield (0.008 g, 76%), mp 171–173 °C (ethanol); ν_{max} (neat) 826, 1159, 1218, 1486, 1508, 1598 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.86 (s, 3H), 4.13 (s, 3H), 6.99 (d, *J* 8.7 Hz, 2H), 7.14–7.24 (m, 5H), 7.72 (t, *J* 8.7 Hz, 2H), 7.84 (t, *J* 8.7 Hz, 2H), 7.90 (d, *J* 1.8 Hz, 1H), 8.06 (d, *J* 8.7 Hz, 2H), 8.32 (d, *J* 1.8 Hz, 1H); δ_C (75 MHz, $CDCl_3$) 55.4, 55.7, 96.7, 114.0, 114.5 (d, ^2J 21.1 Hz), 115.7 (d, ^2J 21.4 Hz), 118.9, 120.9, 128.6, 128.9 (d, $^3J_{CF}$ 8.0 Hz), 129.9, 132.5, 132.6 (d, $^3J_{CF}$ 8.0 Hz), 135.7 (d, $^4J_{CF}$ 2.5 Hz), 136.2, 136.8 (d, $^4J_{CF}$ 3.1 Hz), 139.5, 145.7, 156.8, 160.8, 162.3 (d, $^1J_{CF}$ 244.4 Hz), 162.6 (d, $^1J_{CF}$ 245.3 Hz), 162.9; *m*/*z* (100, MH^+) 454; HRMS (ES): MH^+, found 454.1608. $C_{29}H_{22}NF_2O_2^+$ requires 454.1619.

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