2-Aryl-4-azido-3-(bromo/iodo)quinolines as Substrates for the Synthesis of Primary 4-Amino-2,3-disubstituted Quinoline Derivatives

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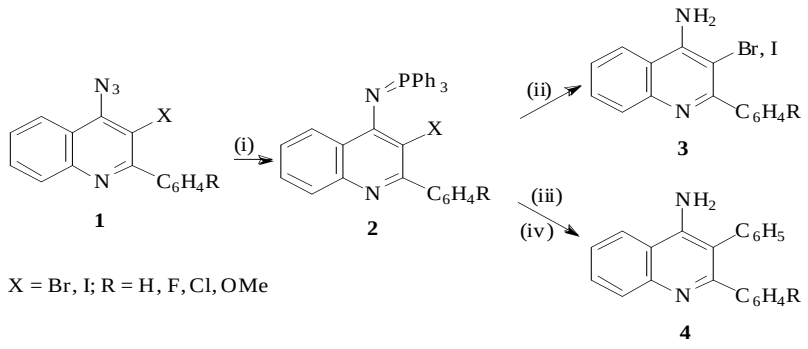

Reagents and conditions: (i) PPh_3, THF, heat, 12h; (ii) 80% acetic acid, heat, 5h; (iii) $PhB(OH)_2$, $Pd(PPh_3)_4$, K_2CO_3 (aq), DMF, heat, 48h (X = I); (iv) 80% acetic acid, heat, 5h

Staudinger reaction of the 2-aryl-4-azido-3-bromoquinolines and 2-aryl-4-azido-3-iodoquinolines with triphenyl phosphine in refluxing tetrahydrofuran afforded series of 2-aryl-3-halogeno-4-(triphenylphosphoranylideneamino)quinolines. The latter were, in turn, hydrolyzed to the corresponding primary 4-amino-2-aryl-3-(bromo/iodo)quinolines using 80% acetic acid under reflux. Tetrakis(triphenylphosphine)-palladium(0)–catalyzed Suzuki reaction of the 2-aryl-3-iodo-4-(triphenylphosphoranylideneamino)-quinolines with phenylboronic acid in dimethyl formamide in the presence of 2 *M* K_2CO_3 followed by hydrolysis of the incipient 2,3-diaryl-4-(triphenylphosphoranylideneamino)quinolines with 80% acetic acid afforded the 4-amino-2,3-diarylquinolines.

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INTRODUCTION

4-Aminoquinolines represent an important class of compounds and have attracted a great deal of attention in recent years because of their pharmacological properties [1-3]. They are known to serve as antimalarial, anti-inflammatory, antibacterial, and antihypertensive agents [1] as well as immuno-stimulants [2a] and non-nucleoside HIV-1 inhibitors [2b]. It is reported that over-activation of *N*-methyl-D-aspartate (NMDA) subtype of central excitatory amino acid receptors play a role in numerous neuro-degenerative disorders, for example, it delays neuronal loss following cerebral ischaemia, epilepsy, Alzheimer's diseases and AIDS related dementia [3a]. 4-Amino-2-arylquinolines have been found to represent a novel class of NR1/2B subtype selective NMDA receptor antagonists [3b]. Several methods continue to appear in literature describing the synthesis of primary 4-amino-2-arylquinolines and most involve deprotection of 4-(*p*-methoxyphenyl)aminoquinolines [4], 4-benzylamino-2-arylquinolines [5] or *N*,*N*-bis(trimethylsilyl)-2-phenylquinolin-4-amine [6] using cerium(IV) ammonium nitrate in acetonitrile, boron tribromide in dichloromethane or tetrabutylammonium fluoride, respectively. Several derivatives have also been prepared through reduction of 4-azidoquinolines derived from quinoline derivatives bearing a leaving group such as tosyloxy or halogen using sodium azide [7] or from the 4-oxo precursors using diphenylphosphorylazide [8]. We have also synthesized 4-amino-2-arylquinolines *via* sodium ethoxide-promoted Neber rearrangement of O-mesyloximes derived from the 2-aryl-1-methylsulfonyl-2,3-dihydroquinolin-4(1*H*)-ones [9]. Although several methods have been developed before for the synthesis of 4-amino-2-arylquinolines corresponding data for the synthesis of 2,3-disubstituted primary 4-aminoquinolines is considerably less documented [5,8].

In our continuing efforts to introduce exhaustive substitution into the 2-arylquinoline moiety, we required an efficient method for the synthesis of 4-

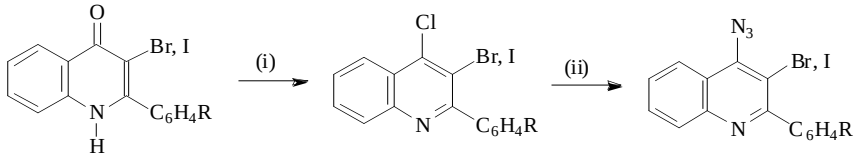
amino-2-arylquinolines bearing a halogen at the 3-position of the heterocyclic framework because of the profound effect a halogen atom can have on the physical, chemical and biological properties of such systems. We now report that Staudinger reaction of 2-aryl-4-azido-3-(bromo/iodo)quinolines with triphenyl phosphine in refluxing THF followed by acetic acid–promoted hydrolysis of the incipient 2-aryl-3-halogeno-4-(triphenylphosphoranylideneamino)quinolines may provide a versatile, new approach to primary 4-amino-2-aryl-3-halogenoquinolines. Moreover, palladium–catalyzed Suzuki–Miyaura coupling of the 2-aryl-3-iodo-4-(triphenylphosphoranylideneamino)quinolines with phenylboronic acid followed by hydrolysis afforded 4-amino-2,3-diarylquinolines.

RESULTS AND DISCUSSION

In the first part of this investigation, we subjected the previously described 2-aryl-3-halogenoquinolin-4(1*H*)-ones **1** (X = Br, I) [10] to phosphoryl chloride under reflux to afford series of the known 2-aryl-3-bromo-4-chloroquinolines (**2a-d**) [10b] and the previously undescribed 2-aryl-4-chloro-3-iodoquinoline derivatives (**2e-h**) (Scheme 1). Attempted nucleophilic displacement of 4-chloro substituent from the 2-aryl-3-halogenoquinolines with benzylamine in phenol under reflux in analogy with literature procedure for the synthesis of 4-(benzylamino)-7-methoxy-2-phenylquinoline from 4-chloro-7-methoxyquinoline [11] led in all cases to complete decomposition of the substrate. We then resorted to literature method that involves displacement of chlorine at the γ-position of the quinoline nucleus by azide ion to form azidoquinoline derivatives under very mild conditions [7,12]. The 2-aryl-4-chloro-3-halogenoquinolines (**2a-h**) were subjected to NaN_3 in DMF at room temperature to afford the corresponding hitherto unknown 2-aryl-4-azido-3-halogenoquinoline derivatives (**3a-h**) in reasonable yields (Scheme 1). The presence of the azido group in systems (**3**) is confirmed by strong ir absorption bands in the regions ν_{max} 2116.3 – 2119.0 cm^{-1} (asymmetric) and ν_{max} 1226.7 – 1258.0 cm^{-1} (symmetric) in agreement with the literature values for organic azides [13].

There are several reagents and conditions described in literature for the reduction of azides to primary amines and these include the use of lithium aluminum hydride, sodium borohydride, sodium borohydride/phase-transfer catalyst, catalytic hydrogenation, triethyl phosphite and electrolysis [7,14]. Staudinger reaction involving reaction of azides with triphenyl phosphine followed by acid hydrolysis has been shown to reduce azides to primary amines in the presence of cyano, halogen or carbonyl groups [7]. We required a method that would reduce the azido group to amino functionality without promoting possible reductive removal of 3-halogen atoms that could be observed with most of the reducing agents or conditions described above [7,15]. Consequently, in this investigation we opted for the use of Staudinger reaction conditions and subjected the azido derivatives (**3a**-**h**) to triphenyl phosphine in tetrahydrofuran under reflux and isolated the corresponding 2-aryl-3-halogeno-4-(triphenylphosphoranylideneamino)quinolines (**4**) (Scheme 2). Aryliminophosphoranes ($RN=PPh_3$, R = aryl) are known to be generally stable in air and often in water, but to hydrolyze readily in dilute acid or base [16]. We observed no hydrolysis products when we conducted Staudinger reaction in aqueous THF and attempted hydrolysis of the iminophosphorane using dilute sodium hydroxide in THF-methanol mixture led to the recovery of starting material. We then resorted to the use of dilute acetic acid under reflux and converted the iminophosphoranes (**4**) to the corresponding previously undescribed primary 4-amino-2-aryl-3-halogenoquinolines (**5**)

Scheme 1



(1) (R = H, F, Cl, OCH_3) **(2)** **(3)**

Reagents and conditions: (i) $POCl_3$, heat, 3h; (ii) NaN_3, DMF, r.t., 48h

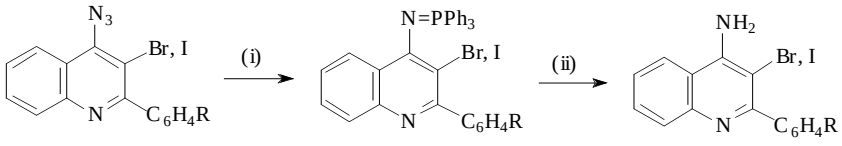
1 - 3	a	b	c	d	e	f	g	h
X	Br	Br	Br	Br	I	I	I	I
R	H	4-F	4-Cl	4-OCH_3	H	4-F	4-Cl	4-OCH_3

(Scheme 2). The ^{1}H nmr spectra of systems (**5**) are characterized by a broad singlet in the region δ 5.40 – 5.50 ppm corresponding to the amino group and a set of signals in the aromatic region. The presence of the amino group in these compounds is further confirmed by the ir absorption bands in the region ν_{max} 3060 – 3430 cm^{-1}.

4-amino-2,3-diarylquinolines (**7**) using 80% acetic acid under reflux (Scheme 3).

In summary, the observed results of Staudinger reaction of the 2-aryl-4-azido-3-halogenoquinolines and subsequent hydrolysis of the resulting 2-aryl-3-halogeno-4-(triphenylphosphoranylideneamino)quinolines represents convenient synthetic strategy for the

Scheme 2



(3) **(4)** **(5)**

Reagents and conditions: (i) PPh_3, THF, heat, 12h; (ii) AcOH (aq), heat, 7h

4 - 5	**a**	**b**	**c**	**d**	**e**	**f**	**g**	**h**
X	Br	Br	Br	Br	I	I	I	I
R	H	4-F	4-Cl	4-OCH_3	H	4-F	4-Cl	4-OCH_3

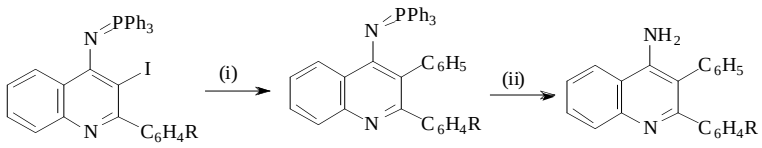
Among all C-C bond forming cross-coupling processes, Suzuki–Miyaura reaction which involves palladium–catalyzed cross-coupling of aryl halides with organoboronic acids in the presence of a base is one of the versatile procedures for the synthesis of unsymmetrical biaryl derivatives [17]. In our continuing efforts to introduce exhaustive substitution into 2-arylquinoline moiety, we subjected the 3-iodoquinoline derivatives (**4e**–**h**) to cross-coupling reaction with phenylboronic acid in the presence of $Pd(PPh_3)_4$ and 2 *M* K_2CO_3 in refluxing DMF. The 2,3-diaryl-4-(triphenylphosphoranylideneamino)quinolines **6** were isolated as sole products and in high yields with or without any need for column chromatography. Systems (**6**) were, in turn, hydrolyzed to the corresponding previously undescribed primary

construction of 3-halogenated 4-amino-2-arylquinolines of potential biological interest that can be obtainable only with difficulty otherwise. The 3-iodoquinoline moiety also provides an important functional group that could facilitate other transition metal-mediated carbon–carbon bond formation. Further studies of chemical transformation and biological activity of the products prepared in this investigation are currently under way in our laboratory.

EXPERIMENTAL

Melting points were recorded on a Thermocouple digital melting point apparatus and are uncorrected. Nmr spectra were obtained as $CDCl_3$ or DMSO-d_6 solutions using Varian Mercury 300 MHz NMR spectrometer and the chemical shifts are quoted relative to the solvent peaks. The ir spectra were recorded as

Scheme 3



(4) **6)** **(7)**

Reagents and conditions: (i) $PhB(OH)_2$, $Pd(PPh_3)_4$, K_2CO_3(aq), DMF, heat, 48h; (ii) 80% AcOH, heat, 7h.

(6), (7)	**a**	**b**	**c**	**d**
R	H	4-F	4-Cl	4-OCH_3

powder using FTS 7000 Series Digilab Win-IR Pro spectrometer. Low-resolution and high-resolution (EI) mass spectra were recorded on a VG70-SEQ double-focusing magnetic sector spectrometer (University of Northwest, Potchefstroom campus). Elemental analysis was performed at the Department of Chemistry of the University of Cape Town. The synthesis and characterization of substrates **(1a-d)** [10a] and **(2a-d)** [10b] have been described elsewhere. Substrates **(2e-h)** which are new were prepared as follows:

General Procedure for the Reactions of 2-Aryl-3-iodoquinolin-4(1*H*)-ones (1) with $POCl_3$. A stirred mixture of 2-aryl-3-iodoquinolin-4-(1*H*)-one **(1)** (1 equiv.) and phosphoryl chloride (5 mL per mmol of **(1)**) was heated under reflux for 3 hours. The cooled mixture was transferred to a volumetric flask and then quenched slowly with ice-cold water. After 30 minutes, the mixture was neutralized with ammonia solution and stirred vigorously at room temperature. The resulting precipitate was filtered and recrystallized to afford the corresponding 2-aryl-4-chloro-3-iodoquinoline **(2)**.

4-Chloro-3-iodo-2-phenylquinoline (2e). This compound was obtained as white solid (55%) m.p. 150 – 153°C (ethyl acetate); ^{1}H nmr (300 MHz, DMSO-d_6): δ 7.47 – 7.58 (5H, m), 7.77 (1H, dt, *J* = 1.5 and 7.8 Hz), 7.91 (1H, dt, *J* = 1.2 and 7.8 Hz), 8.07 (1H, d, *J* = 8.4 Hz), 8.26 (1H, dd, *J* = 0.9 and 8.4 Hz); ^{13}C nmr (75 MHz, DMSO-d_6): δ 99.2, 124.7, 125.0, 127.8, 128.7, 129.0, 129.1, 129.4, 131.3, 143.2, 146.5, 146.6, 162.5; ir (neat): ν_{max}/cm^{-1} 762, 845, 1026, 1088, 1339, 1555; ms (EI) m/z 365 (M$^+$, 83), 238 (100), 220 (69), 203 (58). Hrms (EI) calculated for $C_{15}H_9N^{35}ClI$: 364.9477. Found: 364.9468. *Anal. calc*. for $C_{15}H_9N^{35}ClI$: C, 49.37; H, 2.49; N, 3.84. Found: C, 49.08; H, 2.48; N, 3.47.

4-Chloro-2-(4-fluorophenyl)-3-iodoquinoline (2f). This compound was obtained as white solid (62%) m.p. 176 – 178°C (ethyl acetate); ^{1}H nmr (300 MHz, DMSO-d_6): δ 7.35 (2H, *J* = 9.0 Hz), 7.64 (2H, dd, *J* = 5.7 and 9.0 Hz), 7.78 (1H, dt, *J* = 1.2 and 7.8 Hz), 7.92 (1H, dt, *J* = 1.5 and 7.8 Hz), 8.08 (1H, d, *J* = 9.0 Hz), 8.27 (1H, dd, *J* = 0.6 and 8.7 Hz); ^{13}C nmr (75 MHz, DMSO-d_6): δ 99.3, 114.7 (d, $^2J_{CF}$ = 21.6 Hz), 124.7, 125.0, 129.1, 131.3, 131.4 (d, $^3J_{CF}$ = 8.3 Hz), 139.6 (d, $^4J_{CF}$ = 3.6 Hz), 146.6, 146.7, 161.5, 162.2 (d, $^1J_{CF}$ = 244.8 Hz); ir (neat): ν_{max}/cm^{-1} 758, 828, 1219, 1343, 1508, 1597; ms (EI) m/z 383 (M$^+$, 94), 256 (100), 221 (73). Hrms (EI) calculated for $C_{15}H_8NF^{35}ClI$: 382.9374. Found 382.9368. *Anal. calc*. for $C_{15}H_8NF^{35}ClI$: C, 47.05; H, 2.11; N, 3.67. Found: C, 47.15; H, 2.05; N, 3.65.

4-Chloro-2-(4-chlorophenyl)-3-iodoquinoline (2g). This compound was obtained as white solid (65%) m.p. 218 – 220°C (ethyl acetate); ^{1}H nmr (300 MHz, DMSO-d_6): δ 7.59 (2H, d, *J* = 8.4 Hz), 7.70 (2H, d, *J* = 8.4 Hz), 7.83 (1H, dt, *J* = 1.5 and 7.5 Hz), 7.94 (1H, dt, *J* = 1.2 and 7.5 Hz), 8.11 (1H, d, *J* = 8.4 Hz), 8.26 (1H, dd, *J* = 0.9 and 8.4 Hz); ^{13}C nmr (75 MHz, DMSO-d_6): δ 99.2, 124.7, 125.0, 127.9, 129.2, 129.4, 131.1, 131.4, 133.5, 142.0, 146.5, 146.8, 161.3; ir (neat): ν_{max}/cm^{-1} 756, 822, 1092, 1247, 1342, 1473, 1605; ms (EI) m/z 399 (M$^+$, 62), 273 (100), 238 (70), 220 (54). Hrms (EI) calculated for $C_{15}H_8N^{35}Cl_2I$: 398.9079. Found: 398.9078. *Anal. calc*. for $C_{15}H_8N^{35}Cl_2I$: C, 45.16; H, 2.02; N, 3.51. Found: C, 44.83; H, 2.02; N, 3.44.

4-Chloro-3-iodo-2-(4-methoxyphenyl)quinoline (2h). This compound was obtained as white solid (56%) m.p. 185 – 187°C (ethyl acetate); ^{1}H nmr (300 MHz, DMSO-d_6): δ 3.84 (3H, s), 7.05 (2H, d, *J* = 9.0 Hz), 7.54 (2H, d, *J* = 9.0 Hz), 7.75 (1H, tt, *J* = 1.5 and 8.0 Hz), 7.89 (1H, tt, *J* = 1.5 and 7.5 Hz), 8.05 (1H, d, *J* = 7.8 Hz), 8.24 (1H, d, *J* = 8.3 Hz); ^{13}C nmr (75 MHz, DMSO-d_6): δ 55.4, 98.2, 113.3, 125.1, 125.7, 128.2, 129.7, 130.6, 130.9, 136.0, 147.3, 147.7, 160.1, 162.2; ir (neat): ν_{max}/cm^{-1} 760, 824, 1030, 1177, 1246, 1511, 1606; ms (EI) m/z 395 (M$^+$, 6), 269 (100), 254 (69), 191 (24), 162 (27), 127 (32). Hrms (EI) calculated for $C_{16}H_{11}NO^{35}ClI$: 394.9568. Found: 394.9574. *Anal. calc*. for $C_{16}H_{11}NO^{35}ClI$: C, 48.66; H, 2.81; N, 3.55. Found: C, 48.41; H, 2.69; N, 3.40.

General procedure for the Reaction of (2a-h) with sodium azide in DMF. A stirred mixture of **(2)** (1 equiv.) and sodium azide (1.5 equiv.) in DMF (5mL per mmol of **(2)**) was stirred at room temperature for 48 hours with the exclusion of moisture. The mixture was poured into ice-cold water and the resulting precipitate was collected by filtration and recrystallized to afford 2-aryl-4-azido-3-halogenoquinoline **(3)**.

4-Azido-3-bromo-2-phenylquinoline (3a). This compound was obtained as solid (65%) m.p. 124 – 126°C (ethanol); ^{1}H nmr (300 MHz, $CDCl_3$): δ 7.46 – 7.53 (3H, m), 7.59 (1H, dt, *J* = 1.2 and 7.8 Hz), 7.63 – 7.68 (2H, m), 7.76 (1H, dt, *J* = 1.2 and 8.7 Hz), 8.09 (1H, d, *J* = 8.4 Hz), 8.21 (1H, d, *J* = 8.7 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 111.5, 122.5, 123.0, 127.4, 128.0, 128.9, 129.2, 129.5, 130.6, 140.1, 142.7, 146.9, 159.6; ir (neat): ν_{max}/cm^{-1} 765, 1380, 1481, 1566, 2114; ms (EI) m/z 324 (M$^+$, 5%), 298 (40), 296 (28), 219 (46), 217 (100), 190 (32), 89 (36). Hmrs (EI) calculated for $C_{15}H_9N_4{}^{79}Br$: 324.0016. Found: 324.0005. *Anal. calc*. for $C_{15}H_9N_4{}^{79}Br$: C, 55.61; H, 2.80; N, 17.29. Found: C, 55.33; H, 2.76; N, 17.07.

4-Azido-3-bromo-2-(4-fluorophenyl)quinoline (3b). This compound was obtained as solid (70%) m.p. 177 – 179°C (ethanol); ^{1}H nmr (300 MHz, $CDCl_3$): δ 7.18 (2H, t, *J* = 8.7 Hz), 7.60 (1H, dt, *J* = 1.2 and 7.8 Hz)), 7.66 (2H, t, *J* = 7.8 Hz), 7.76 (1H, dt, *J* = 1.5 and 7.8 Hz), 8.07 (1H, d, *J* = 8.4 Hz), 8.21 (1H, dd, *J* = 0.9 and 8.2 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 111.4, 115.2 (d, $^2J_{CF}$ = 21.6 Hz), 122.6, 123.1, 127.7, 129.6, 130.8, 131.3 (d, $^3J_{CF}$ = 8.3 Hz), 136.1 (d, $^4J_{CF}$ = 3.4 Hz), 143.0, 146.9, 158.6, 163.2 (d, $^1J_{CF}$ = 247.3 Hz); ir (neat): ν_{max}/cm^{-1} 752, 826, 1160, 1222, 1377, 1580, 1600, 2115; ms (EI) m/z 343 (M$^+$, 10), 342 (45), 316 (65), 256 (30), 236 (48), 235 (100), 208 (52), 107 (71). Hmrs (EI) calculated for $C_{15}H_8N_4F^{79}Br$: 343.9895. Found: 343.9859. *Anal. calc*. for $C_{15}H_8N_4F^{79}Br$: C, 52.37; H, 2.34; N, 16.28. Found: C, 51.48; H, 2.18; N, 16.35.

4-Azido-3-bromo-2-(4-chlorophenyl)quinoline (3c). This compound was obtained as solid (73%) m.p. 170 – 172°C (ethanol); ^{1}H nmr (30 MHz, $CDCl_3$): δ 7.47 (2H, d, *J* = 8.7 Hz), 7.58 – 7.64 (3H, m), 7.77 (1H, t, *J* = 7.8 Hz), 8.07 (1H, d, *J* = 8.4 Hz), 8.21 (1H, d, *J* = 8.3 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): 111.2, 122.6, 123.1, 127.8, 128.4, 129.6, 130.8, 130.9, 135.1, 138.5, 143.0, 146.9, 158.5; ir (neat): ν_{max}/cm^{-1} 757, 824, 1096, 1222, 1380, 1479, 1508, 2114; ms (EI) m/z 360 (M$^+$, 4), 316 (42), 271 (37), 237 (41), 235 (100). Hmrs (EI) calculated for $C_{15}H_8N_4{}^{35}Cl^{79}Br$: 359.9970. Found: 359.9978. *Anal. calc*. for $C_{15}H_8N_4{}^{35}Cl^{79}Br$: C, 50.05; H, 2.24; N, 15.56. Found: C, 49.48; H, 2.03; N, 15.74.

4-Azido-3-bromo-2-(4-methoxyphenyl)quinoline (3d). This compound was obtained as solid (80%) m.p. 169 – 171°C (ethanol); ^{1}H nmr (300 MHz, $CDCl_3$): δ 3.87 (3H, s), 7.02 (2H, d, *J* = 8.2 Hz), 7.57 (1H, t, *J* = 7.7 Hz), 7.65 (2H, d, *J* = 8.4 Hz), 7.74 (1H, t, *J* = 7.2 Hz), 8.07 (1H, d, *J* = 8.1 Hz), 8.19 (1H, d, *J* = 8.4 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 55.3, 111.8, 113.4, 122.5, 122.9, 127.3, 129.5, 130.6, 130.8, 132.5, 142.8, 146.9, 159.2, 160.1; ir (neat): ν_{max}/cm^{-1} 745, 818, 1026, 1173, 1246,

1373, 1512, 1558, 1610, 2111; ms (EI) m/z 354 (M^+, 15), 328 (21), 249 (43), 247 (57), 86 (60), 84 (100). Hmrs (EI) calculated for $C_{16}H_{11}N_4O^{79}Br$: 354.0120. Found: 354.0109. *Anal. calc.* for $C_{16}H_{11}N_4O^{79}Br$: C, 54.28; H, 3.13; N, 15.83. Found: C, 53.97; H, 2.87; N, 15.67.

4-Azido-3-iodo-2-phenylquinoline (3e). This compound was obtained as solid (60%) m.p. 137 – 140°C (ethanol); ^{1}H nmr (300 MHz, $CDCl_3$): δ 7.46 – 7.51 (3H, m), 7.55 – 7.59 (2H, m), 7.62 (1H, dt, *J* = 1.2 and 7.7 Hz), 7.63 (1H, dt, *J* = 1.2 and 8.4 Hz), 7.78 (1H, dt, *J* = 1.5 and 7.7 Hz), 8.23 (1H, td, *J* = 0.6 and 8.5 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 88.4, 121.8, 122.9, 127.6, 128.0, 128.9, 129.1, 129.9, 130.9, 142.8, 146.8, 147.8, 162.8; ir (neat): ν_{max}/cm^{-1} 698, 764, 1258, 1374, 1479, 2111; ms (EI) m/z 372 (M^+, 32), 344 (63), 317 (100), 190 (33), 89 (37). Hmrs (EI) calculated for $C_{15}H_9N_4I$: 371.9869. Found: 371.9872. *Anal. calc.* for $C_{15}H_9N_4I$: C, 48.43; H, 2.44; N, 15.06. Found: C, 48.22; H, 2.36; N, 14.59.

4-Azido-2-(4-fluorophenyl)-3-iodoquinoline (3f). This compound was obtained as solid (75%) m.p. 169 – 170°C (ethanol); ^{1}H nmr (300 MHz, $CDCl_3$) δ 7.14 (2H, m), 7.53 – 7.63 (3H, m), 7.76 (1H, dt, *J* = 1.5 and 7.1 Hz), 8.08 (1H, d, *J* = 8.4 Hz), 8.19 (1H, dd, *J* 1.2 and 8.4 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 88.2, 115.5 (d, $^2J_{CF}$ 21.6 Hz), 121.8, 122.8, 127.7, 129.7, 131.0, 131.1 (d, $^3J_{CF}$ = 8.6 Hz), 138.6 (d, $^4J_{CF}$ = 3.4 Hz), 146.9, 147.7, 161.7, 163.0 (d, $^1J_{CF}$ = 247.1 Hz); ir (neat): ν_{max}/cm^{-1} 761, 834, 1227, 1369, 1477, 1510, 1600, 2116; ms (EI) m/z 390 (M^+, 23), 362 (51), 235 (100), 208 (27), 107 (41). Hmrs (EI) calculated for $C_{15}H_8N_4FI$: 389.9783. Found: 389.9778. *Anal. calc.* for $C_{15}H_8N_4FI$: C, 46.20; H, 2.07; N, 14.27. Found: C, 46.23; H, 2.08; N, 14.66.

4-Azido-2-(4-chlorophenyl)-3-iodoquinoline (3g). This compound was obtained as solid (78%) m.p. 173 – 175°C (ethanol); ^{1}H nmr (300 MHz, $CDCl_3$) δ 7.46 (2H, d, *J* = 8.4 Hz), 7.55 (2H, d, *J* = 8.4 Hz), 7.63 (1H, dt, *J* = 1.2 and 8.4 Hz), 7.79 (1H, dt, *J* = 1.2 and 7.4 Hz), 8.10 (1H, td, *J* = 0.6 and 8.4 Hz), 8.30 (1H, td, *J* = 0.6 and 8.5 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 87.8, 121.9, 122.9, 127.8, 128.3, 129.9, 130.7, 131.0, 135.0, 141.1, 147.0, 147.8, 161.6; ir (neat): ν_{max}/cm^{-1} 761, 827, 1092, 1233, 1369, 1480, 2118; ms (EI) m/z 406 (M^+, 24), 378 (49), 251 (100), 216 (29), 123 (35). Hmrs (EI) calculated for $C_{15}H_8N_4{}^{35}ClI$: 405.9482. Found: 405.9482. *Anal. calc.* for $C_{15}H_8N_4{}^{35}ClI$: C, 44.38; H, 1.98; N, 13.80. Found: C, 44.60; H, 1.81; N, 14.19.

4-Azido-3-iodo-2-(4-methoxyphenyl)quinoline (3h). This compound was obtained as solid (67%) m.p. 137 – 140°C (ethanol); ^{1}H nmr (300 MHz, $CDCl_3$): δ 3.88 (3H, s), 7.01 (2H, d, *J* = 9.0 Hz), 7.57 (2H, d, *J* = 8.7 Hz), 7.60 – 7.80 (1H, m), 7.77 (1H, dt, *J* = 1.5 and 7.6 Hz), 8.11 (1H, d, *J* = 8.6 Hz), 8.16 (1H, dd, *J* = 0.9 and 8.6 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 55.4, 88.8, 113.4, 121.9, 122.8, 127.4, 129.8, 130.7, 130.8, 135.3, 146.8, 147.9, 160.1, 162.4; ir (neat): ν_{max}/cm^{-1} 760, 826, 1034, 1176, 1247, 1369, 1513, 1605, 2115; ms (EI) m/z 402 (M^+, 59), 374 (17), 247 (100), 204 (22), 119 (25). Hmrs (EI) calculated for $C_{16}H_{11}N_4OI$: 401.9835. Found: 401.9834. *Anal. calc.* for $C_{16}H_{11}N_4OI$: C, 47.80; H, 2.77; N, 13.94. Found: C, 47.40; H, 3.05; N, 13.46.

General Procedure for the Reactions of (3) with PPh_3 in THF. A stirred mixture of **(3)** (1 equiv.) and PPh_3 (3 equiv.) in THF (5mL per mmol of **(3)**) was refluxed for 5 hours. The mixture was evaporated under reduced pressure and the residue was purified by column chromatography, first with benzene or toluene to remove excess triphenyl phosphine followed by elution of the product with ethyl acetate. The following products were prepared:

3-Bromo-2-phenyl-4-(triphenylphosphoranylideneamino)-quinoline (4a). This compound was obtained as solid (75%) m.p. 170 – 172°C; ^{1}H nmr (300 MHz, $CDCl_3$): δ 7.17 (1H, dt, *J* = 1.2 and 8.1 Hz), 7.33 – 7.56 (15H, m), 7.70 – 7.78 (6H, m), 7.97 (1H, d, *J* = 8.1 Hz), 8.10 (1H, d, *J* = 7.8 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 112.5 (d, $^4J_{CP}$ = 10.8 Hz), 124.6, 125.6, 125.9, 126.0, 127.6, 127.8, 128.5 (d, $^3J_{CP}$ = 12.5 Hz), 128.8, 129.0, 131.7 (d, $^1J_{CP}$ = 104.7 Hz), 131.4 (d, $^4J_{CP}$ = 2.9 Hz), 132.5 (d, $^2J_{CP}$ = 10.0 Hz), 142.6, 147.4, 154.3, 159.8; ^{31}p nmr: δ 2.78; ir (neat): ν_{max}/cm^{-1} 749, 990, 1113, 1217, 1359, 1419, 1479, 1526, 1557; ms (EI) m/z 559 (70), 558 (M^+, 71), 557 (33), 480 (37), 479 (100), 262 (36), 183 (81). Hmrs (EI) calculated for $C_{33}H_{24}N_2{}^{79}BrP$: 558.0860. Found: 558.0860. *Anal. calc.* for $C_{33}H_{24}N_2{}^{79}BrP$: C, 71.02; H, 4.33; N, 5.02. Found: C, 70.78; H, 3.83; N, 4.67.

3-Bromo-2-(4-fluorophenyl)-4-(triphenylphosphoranyl-ideneamino)quinoline (4b). This compound was obtained as solid (80%) m.p. 184 – 186°C. ^{1}H nmr (300 MHz, $CDCl_3$): δ 7.06 (2H, t, *J* = 8.4 Hz), 7.17 (1H, dt, *J* = 1.5 and 7.7 Hz), 7.41 – 7.58 (12H, m), 7.69 – 7.77 (6H, m), 7.96 (1H, d, *J* = 8.4 Hz), 8.09 (1H, dd, *J* = 1.2 and 8.4 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 112.5 (d, $^4J_{CP}$ = 8.0 Hz), 114.5 (d, $^2J_{CF}$ = 21.4 Hz), 124.7, 125.7, 127.8, 127.9, 128.6 (d, $^3J_{CP}$ = 12.5 Hz), 128.9, 129.0, 131.0 (d, $^3J_{CF}$ = 8.3 Hz), 131.6 (d, $^1J_{CP}$ = 104.8 Hz), 131.8 (d, $^4J_{Cp}$ = 2.9 Hz), 132.4 (d, $^2J_{CP}$ = 10.0 Hz), 138.7 (d, $^4J_{CF}$ = 3.1 Hz), 147.4, 158.7 (d, $^5J_{CP}$ = 1.7 Hz), 162.5 (d, $^1J_{CF}$ = 245.0 Hz); ^{31}p nmr: δ 3.01; ir (neat): ν_{max}/cm^{-1} 750, 826, 990, 1108, 1202, 1360, 1395, 1431, 1474, 1506, 1555; ms (EI) m/z 578 (M^+, 64), 498 (40), 497 (100), 262 (43), 183 (86). Hmrs (EI) calculated for $C_{33}H_{23}N_2F^{79}BrP$: 576.0773. Found: 576.0770. *Anal. calc.* for $C_{33}H_{23}N_2F^{79}BrP$: C, 68.80; H, 4.02; N, 4.86. Found: C, 68.43; H, 3.98; N, 4.67.

3-Bromo-2-(4-chlorophenyl)-4-(triphenylphosphoranyl-ideneamino)quinoline (4c). This compound was obtained as solid (85%) m.p. 220 – 222°C; ^{1}H nmr (300 MHz, $CDCl_3$): δ 7.17 (1H, dt, *J* = 1.2 and 7.8 Hz), 7.34 (1H, *J* = 8.4 Hz), 7.42 – 7.59 (12H, m), 7.69 – 7.77 (7H, m), 7.95 (1H, d, *J* = 8.4Hz), 8.09 (1H, dd, *J* = 0.9 and 8.4 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 112.2 (d, $^4J_{CP}$ = 8.0 Hz), 124.8, 125.7, 127.8, 128.0, 128.2, 128.6 (d, $^3J_{CP}$ = 12.5 Hz), 129.0, 130.6, 131.6 (d, $^1J_{CP}$ = 105.0 Hz), 131.8 (d, $^4J_{CP}$ = 2.9 Hz), 132.3, 132.5 (d, $^2J_{CP}$ = 10.2 Hz), 133.8, 141.0, 147.4, 154.5, 158.5; ^{31}p nmr: δ 3.09; IR (neat): ν_{max}/cm^{-1} 742, 990, 1109, 1200, 1395, 1431, 1477; ms (EI) m/z 594 (M^+, 74), 592 (51), 515 (42), 514 (57), 513 (100), 277 (58), 262 (46), 183 (97). Hmrs (EI) calculated for $C_{33}H_{23}N_2{}^{35}Cl^{79}BrP$: 592.0462. Found: 592.0455. *Anal. calc.* for $C_{33}H_{23}N_2{}^{35}Cl^{79}BrP$: C, 66.95; H, 3.92; N, 4.73. Found: C, 66.38; H, 3.95; N, 4.34.

3-Bromo-2-(4-methoxyphenyl)-4-(triphenylphosphoranyl-ideneamino)quinoline (4d). This compound was obtained as solid (76%) m.p. 208 – 210°C; ^{1}H nmr (300 MHz, $CDCl_3$): δ 3.82 (3H, s), 6.91 (2H, d, *J* = 9.0 Hz), 7.15 (1H, dt, *J* = 1.2 and 7.8 Hz), 7.43 – 7.50 (6H, m), 7.51 – 7.58 (6H, m), 7.69 – 7.78 (6H, m), 7.98 (1H, d, *J* = 8.1Hz), 8.07 (1H, dd, *J* = 1.5 and 8.6 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 55.3, 113.0 (2 x C), 127.7, 127.8, 128.5 (d, $^3J_{CP}$ = 12.5 Hz), 128.7, 128.9, 130.5, 131.0, 131.8 (d, $^4J_{CP}$ = 2.9 Hz), 131.7 (d, $^1J_{CP}$ = 104.4 Hz), 132.4, 132.5 (d, $^2J_{CP}$ = 10.0 Hz), 135.3, 147.4, 159.3; ^{31}P nmr: δ 2.70; ir (neat): ν_{max}/cm^{-1} 747, 827, 991, 1107, 1248, 1356, 1433, 1479, 1510, 1557, 1606; ms (EI) m/z 588 (M^+, 83), 587 (40), 510 (43),

277 (58), 262 (66), 249 (45), 183 (100). Hmrs (EI) calculated for $C_{34}H_{26}N_2O^{79}BrP$: 588.1066. Found: 588.1066. *Anal. calc*. for $C_{34}H_{26}N_2O^{79}BrP$: C, 69.44; H, 4.45; N, 4.76. Found: C, 69.49; H, 4.42; N, 4.46.

3-Iodo-2-phenyl-4-(triphenylphosphoranylideneamino)-quinoline (4e). This compound was obtained as solid (84%) m.p. 215 – 217°C; ^{1}H nmr (300 MHz, $CDCl_3$): δ 6.96 (1H, t, *J* = 7.8 Hz), 7.34 – 7.58 (15H, m), 7.70 – 7.78 (7H, m), 7.96 (1H, d, *J* = 8.4 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 95.1 (d, $^4J_{CP}$ = 10.8 Hz), 124.3, 125.8, 125.9, 126.0, 127.6, 127.7, 128.5 (d, $^3J_{CP}$ = 12.5 Hz), 128.8, 128.9, 130.9 (d, $^1J_{CP}$ = 104.2 Hz), 131.4 (d, $^4J_{CP}$ = 2.9 Hz), 132.7 (d, $^2J_{CP}$ = 10.0 Hz), 145.4, 148.2, 158.1 (d, $^4J_{CP}$ = 2.6 Hz), 163.1; ^{31}P nmr: δ 1.60; ir (neat): ν_{max}/cm^{-1} 748, 984, 1112, 1213, 1348, 1406, 1476, 1516, 1555; ms (EI) m/z 606 (M^+, 47), 479 (100), 262 (28), 183 (49). Hmrs (EI) calculated for $C_{33}H_{24}N_2IP$: 606.1013. Found: 606.0710. *Anal. calc*. for $C_{33}H_{24}N_2IP$: C, 65.40; H, 3.99; N, 4.62. Found: C, 65.39; H, 4.33; N, 4.37.

2-(4-Fluorophenyl)-3-iodo-4-(triphenylphosphoranylidene-amino)quinoline (4f). This compound was obtained as solid (79%) m.p. 215 – 217°C; ^{1}H nmr (300 MHz, $CDCl_3$): δ 6.97 (1H, dt, 1.5 and, *J* = 8.1 Hz), 7.07 (2H, t, 8.7 Hz), 7.41 – 7.50 (9H, m), 7.52 – 7.59 (3H, m), 7.69 – 7.79 (7H, m), 7.92 (1H, d, *J* = 8.1 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 94.9 (d, $^4J_{CP}$ = 10.8 Hz), 114.5 (d, $^2J_{CF}$ = 21.3 Hz), 124.4, 125.8, 125.9. 126.0, 128.6 (d, $^3J_{Cp}$ = 12.5), 128.9, 129.0, 130.8 (d, $^3J_{CF}$ = 8.3 Hz), 130.9 (d, $^1J_{CP}$ = 104.4 Hz), 131.9 (d, $^4J_{CP}$ = 2.8 Hz), 132.8 (d, $^2J_{CP}$ = 10.2 Hz), 141.4 (d, $^4J_{CF}$ = 3.2 Hz), 158.3 (d, $^4J_{CP}$ = 2.8 Hz), 162.0, 162.4 (d, $^1J_{CF}$ = 244.7 Hz); ^{31}P nmr: δ 1.63; ir (neat): ν_{max}/cm^{-1} 744, 834, 987, 1111, 1217, 1352, 1410, 1475, 1504, 1555; ms (EI) m/z 624 (M^+, 48), 498 (38), 497 (100), 183 (46) . Hmrs (EI) calculated for $C_{33}H_{23}N_2FIP$: 624.0624. Found: 624.0625. *Anal. calc*. for $C_{33}H_{23}N_2FIP$: C, 63.51; H, 3.72; N, 4.49. Found: C, 63.20; H, 3.76; N, 4.07.

2-(4-Chlorophenyl)-3-iodo-4-(triphenylphosphoranyl-ideneamino)quinoline (4g). This compound was obtained as solid (95%) m.p. 212 – 213°C; ^{1}H nmr (300 MHz, $CDCl_3$): δ 6.97 (1H, t, *J* = 7.8 Hz), 7.08 (2H, t, *J* = 8.1 Hz), 7.41 – 7.50 (9H, m), 7.55 – 7.59 (3H, m), 7.69 – 7.782 (7H, m), 7.94 (1H, d, *J* = 8.4 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 94.5 (d, $^4J_{CP}$ = 10.8 Hz), 124.5, 125.8, 125.9, 126.0, 127.8, 128.6 (d, $^3J_{CP}$ = 12.5 Hz), 128.9, 129.0, 130.5, 130.9 (d, $^1J_{CP}$ = 104.4 Hz), 132.0 (d, $^4J_{CP}$ = 2.6 Hz), 132.8 (d, $^2J_{CP}$ = 10.2 Hz), 133.7, 143.7, 148.2, 158.4, 161.8; ^{31}P nmr: δ 1.82; ir (neat): ν_{max}/cm^{-1} 751, 822, 986, 1106, 1194, 1385, 1431, 1476, 1553; ms (EI) m/z 642 (46), 640 (M^+, 91), 513 (100), 262 (48), 183 (85. Hmrs (EI) calculated for $C_{33}H_{23}N_2{}^{35}ClIP$: 640.0325. Found: 640.0330. *Anal. calc*. for $C_{33}H_{23}N_2{}^{35}ClIP$: C, 61.93; H, 3.62; N, 4.38. Found: C, 62.09; H, 3.88; N, 4.17.

3-Iodo-2-(4-methoxyphenyl)-4-(triphenylphosphoranyl-ideneamino)quinoline (4h). This compound was obtained as solid (90%) m.p. 204 – 206 °C; ^{1}H nmr (300 MHz, $CDCl_3$): δ 3.83 (3H, s), 6.89 – 6.98 (3H, m), 7.41 – 7.48 (9H, m), 7.52 – 7.58 (3H, m), 7.69 – 7.78 (7H, m), 7.93 (1H, d, *J* = 8.1 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 55.3, 95.5 (d, $^4J_{CP}$ = 10.8 Hz), 113.0 (2 x C), 124.2, 125.9, 128.6 (d, $^3J_{CP}$ = 12.2 Hz), 128.7, 128.9, 130.5, 131.0 (d, $^1J_{CP}$ = 104.4 Hz), 131.9 (d, $^4J_{CP}$ = 2.6 Hz), 132.8 (d, $^2J_{CP}$ = 10.2 Hz), 137.9, 148.1, 158.3, 159.3, 162.6 ;^{31}P nmr: δ 1.47; ir (neat): ν_{max}/cm^{-1} 757, 826, 989, 1026, 1176, 1244, 1354, 1430, 1477, 1510, 1558, 1609; ms (EI) m/z 636 (M^+, 100), 509 (87), 262 (42), 183 (64). Hmrs (EI) calculated for $C_{34}H_{26}N_2OIP$: 636.0828. Found: 636.0829. *Anal. calc*. for $C_{34}H_{26}N_2OIP$: C, 64.20; H, 4.12; N, 4.40. Found: C, 64.28; H, 4.18; N, 4.00.

General procedure for the Hydrolysis of (4) with aqueous acetic acid. A stirred solution of **(4)** (1 equiv.) in 80% acetic acid (5 mL per mmol of **(4)**) was boiled under reflux for 7 hours. The mixture was evaporated under reduced pressure and the residue was purified by column chromatography (3:2 hexane-ethyl acetate, v/v) to afford 4-amino-2-aryl-3-halogenoquinoline **5**. Whenever necessary, traces of triphenyl phosphonium oxide were removed by washing the solid product with ice-cold methanol. The following products were prepared:

4-Amino-3-bromo-2-phenylquinoline (5a). This compound was obtained as solid (65%) m.p. 160 – 162°C; ^{1}H nmr (300 MHz, $CDCl_3$): δ 5.45 (2H, br s), 7.42 – 7.52 (4H, m), 7.62 – 7.73 (3H, m), 7.79 (1H, d, *J* = 8.1 Hz), 8.06 (1H, dd, *J* = 0.2 and 8.4 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 100.4, 117.6, 120.2, 125.7, 127.9, 128.5, 129.1, 129.8, 130.0, 141.0, 146.4, 147.3, 158.6; ir (neat): ν_{max}/cm^{-1} 752, 924, 1070, 1383, 1430, 1495, 1573, 1620, 3190, 3319, 3412; ms (EI) m/z 298 (M^+, 25), 219 (100). Hmrs (EI) calculated for $C_{15}H_{11}N_2{}^{79}Br$: 299.1698. Found: 299.1750. *Anal. calc*. for $C_{15}H_{11}N_2{}^{79}Br$: C, 60.22; H, 3.71; N, 9.36. Found: C, 59.87; H, 3.77; N, 9.36.

4-Amino-3-bromo-2-(4-fluorophenyl)quinoline (5b). This compound was obtained as solid (73%) m.p. 196 – 198°C; ^{1}H nmr (300 MHz, $CDCl_3$): δ 5.43 (2H, br s), 7.14 (2H, t, *J* = 8.7 Hz), 7.48 (1H, dt, *J* = 0.9 and 7.7 Hz), 7.61 – 7.65 (2H, m), 7.68 (1H, dt, *J* = 1.2 and 7.8 Hz), 7.75 (1H, d, *J* = 8.4 Hz), 8.02 (1H, d, *J* = 8.4 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 100.3, 114.9 (d, $^2J_{CF}$ = 21.3 Hz), 117.6, 120.2, 125.8, 129.9, 130.0, 131.1 (d, $^3J_{CF}$ = 8.3 Hz), 137.1 (d, $^4J_{CF}$ = 3.4 Hz), 146.4, 147.4, 157.6, 162.9 (d, $^1J_{CF}$ = 246.2 Hz); ir (neat): ν_{max}/cm^{-1} 756, 830, 926, 1155, 1227, 1494, 1573, 1643, 3018, 3280, 3412; ms (EI) m/z 316 (M^+, 17), 237 (50), 219 (72), 149 (86), 57 (100). Hmrs (EI) calculated for $C_{15}H_{10}N_2F^{79}Br$: 317.1603. Found: 317.1570. *Anal. calc*. for $C_{15}H_{10}N_2F^{79}Br$: C, 56.81; H, 3.18; N, 8.83. Found: C, 56.31; H, 3.17; N, 8.72.

4-Amino-3-bromo-2-(4-chlorophenyl)quinoline (5c). This compound was obtained as solid (75%) m.p. 166 – 169°C; ^{1}H nmr (300 MHz, $CDCl_3$): δ 5.41 (2H, br s), 7.44 (2H, d, *J* = 8.4 Hz), 7.50 (1H, t, *J* = 7.8 Hz), 7.60 (2H, d, *J* = 8.3 Hz), 7.68 (1H, t, *J* = 7.8 Hz), 7.75 (1H, d, *J* = 8.1 Hz), 8.01 (1H, d, *J* = 8.4 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 100.1, 117.6, 120.2, 125.9, 128.2, 129.9, 130.1, 130.6, 134.6, 139.5, 146.5, 147.4, 157.4; ir (neat): ν_{max}/cm^{-1} 750, 828, 1090, 1398, 1489, 1596, 3372, 3460; ms (EI) m/z 334 (27), 278 (31), 277 (100), 253 (62). Hmrs (EI) calculated for $C_{15}H_{10}N_2{}^{35}Cl^{79}Br$: 333.6146. Found: 333.6081. *Anal. calc*. for $C_{15}H_{10}N_2{}^{35}Cl^{79}Br$: C, 54.00; H, 3.02; N, 8.40. Found: C, 54.29; H, 3.01; N, 8.64.

4-Amino-3-bromo-2-(4-methoxyphenyl)quinoline (5d). This compound was obtained as solid (80%) m.p. 192 – 194°C; ^{1}H nmr (300 MHz, $CDCl_3$): δ 3.85 (3H, s), 5.37 (2H, br s), 6.99 (2H, d, *J* = 8.7 Hz), 7.47 (1H, dt, *J* = 1.2 and 7.8 Hz), 7.63 (2H, d, *J* = 7.8 Hz), 7.66 (1H, dt, *J* = 1.5 and 7.8 Hz), 7.73 (1H, dd, *J* = 0.3 and 8.7 Hz), 8.02 (1H, dd, *J* = 0.5 and 8.7 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 55.3, 100.7, 113.3, 117.5, 120.1, 125.5, 129.7, 130.0, 130.6, 133.7, 146.5, 147.2, 158.2, 159.8; ir (neat): ν_{max}/cm^{-1} 829, 922, 1026, 1171, 1246, 1429, 1497, 1508, 1574, 1608, 3314, 3422; ms (EI) m/z 330 (M^+, 35), 328 (33), 249 (100), 149 (32), 111 (44), 97 (62), 83 (64), 69 (75). Hmrs (EI) calculated for $C_{16}H_{13}N_2O^{79}Br$: 329.1961. Found: 329.1954. *Anal. calc*. for $C_{16}H_{13}N_2O^{79}Br$: C, 58.37; H, 3.98; N, 8.51. Found: C, 58.35; H, 4.07; N, 8.30.

4-Amino-3-iodo-2-phenylquinoline (5e). This compound was obtained as solid (68%) m.p. 183 – 185°C; ^{1}H nmr (300 MHz, $CDCl_3$): δ 5.50 (2H, br s), 7.41 – 7.56 (6H, m), 7.69 (1H, dt, *J* = 1.5 and 7.8 Hz), 7.78 (1H, dd, *J* = 0.9 and 8.5 Hz), 8.03 (1H, dd, *J* = 0.9 and 8.4 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 78.2, 116.7, 120.3, 125.8, 127.9, 128.4, 128.9, 129.9, 130.1, 143.9, 147.1, 150.3, 162.0; ir (neat): ν_{max}/cm^{-1} 755, 913, 1119, 1279, 1368, 1423, 1492, 1570, 1632, 3061, 3393; ms (EI) m/z 347 (M^+, 14), 346 (75), 219 (100), 57 (56). Hmrs (EI) calculated for $C_{15}H_{11}N_2I$: 346.1703. Found: 346.1706. *Anal. calc*. for $C_{15}H_{11}N_2I$: C, 52.04; H, 3.20; N, 8.09. Found: C, 52.48; H, 3.27; N, 8.24.

4-Amino-2-(4-fluorophenyl)-3-iodoquinoline (5f). This compound was obtained as solid (70%) m.p. 190 – 192°C; ^{1}H nmr (300 MHz, $CDCl_3$): δ 5.50 (2H, br s), 7.13 (2H, t, *J* = 8.7 Hz), 7.45 – 7.56 (3H, m), 7.69 (1H, dt, *J* = 1.5 and 7.5 Hz), 7.77 (1H, dd, *J* = 0.6 and 8.4 Hz), 8.01 (1H, dd, *J* = 0.6 and 8.4 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 80.0, 114.9 (d, $^2J_{CF}$ = 21.7 Hz), 116.6, 120.2, 125.9, 129.9, 130.2, 130.9 (d, $^3J_{CF}$ = 8.3 Hz), 140.0 (d, $^4J_{CF}$ = 3.4 Hz), 147.1, 150.3, 161.1, 162.7 (d, $^1J_{CF}$ = 258.1 Hz); ir (neat): ν_{max}/cm^{-1} 754, 827, 923, 1117, 1185, 1225, 1364, 1489, 1510, 1568, 1634, 3056, 3280, 3391; ms (EI) m/z 365 (M^+, 5), 364 (36), 278 (64), 277 (100), 237 (40) 199 (32). Hmrs (EI) calculated for $C_{15}H_{10}N_2FI$: 364.1608. Found: 364.1611. *Anal. calc*. for $C_{15}H_{10}N_2FI$: C, 49.47; H, 2.77; N, 7.69. Found: C, 49.32; H, 2.37; N, 7.49.

4-Amino-2-(4-chlorophenyl)-3-iodoquinoline (5g). This compound was obtained as solid (65%) m.p. 175 – 177°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.52 (2H, br s), 7.42 – 7.53 (5H, m), 7.70 (1H, dt, *J* = 1.2 and 7.8 Hz), 7.77 (1H, dd, *J* = 1.2 and 8.7 Hz), 8.02 (1H, d, *J* = 8.7 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 77.6, 116.7, 120.3, 125.9, 128.2, 129.8, 130.2, 130.5, 134.4, 142.3, 147.1, 150.4, 160.8; ir (neat): ν_{max}/cm^{-1} 757, 826, 921, 1015, 1088, 1162, 1364, 1431, 1489, 1568, 1610, 3061, 3181, 3305, 3416; ms (EI) m/z 382 (M^+, 30), 380 (86), 278 (33), 277 (82), 252 (100), 218 (55), 97 (51), 71 (59), 57 (81). Hmrs (EI) calculated for $C_{15}H_{10}N_2{}^{35}ClI$: 380.6151. Found: 380.6163. *Anal. calc*. for $C_{15}H_{10}N_2{}^{35}ClI$: C, 47.33; H, 2.65; N, 7.36. Found: C, 47.78; H, 2.85; N, 7.85.

4-Amino-3-iodo-2-(4-methoxyphenyl)quinoline (5h). This compound was obtained as solid (60%) m.p. 184 – 186°C; ^{1}H nmr (300 MHz, $CDCl_3$): δ 3.86 (3H, s), 5.50 (2H, br s), 6.98 (2H, *J* = 8.7 Hz), 7.46 (1H, dt, *J* = 1.2 and 7.8 Hz), 7.52 (2H, d, *J* = 8.7 Hz), 7.67 (1H, dt, *J* = 1.2 and 7.8 Hz), 7.76 (1H, d, *J* = 7.8 Hz), 8.02 (1H, d, *J* = 8.4 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 55.3, 78.6, 113.3, 116.7, 120.2, 125.6, 129.8, 130.0, 130.4, 136.5, 147.1, 150.3, 159.7, 161.6; ir (neat): ν_{max}/cm^{-1} 721, 764, 1117, 1175, 1240, 1433, 1636, 3186, 3301, 3429; ms (EI) m/z 377 (M^+, 17), 376 (100), 250 (27), 249 (92), 234 (36), 206 (38), 97 (47), 83 (42), 71 (51), 57 (71). Hmrs (EI) calculated for $C_{16}H_{13}N_2OI$: 376.1966. Found: 376.1958. *Anal. calc*. for $C_{16}H_{13}N_2OI$: C, 51.08; H, 3.48; N, 7.45. Found: C, 51.31; H, 3.62; N, 7.00.

General procedure for $Pd(PPh_3)_4$ catalyzed cross-coupling reactions of (4) in DMF. 2-Aryl-3-iodo-4-(triphenylphosphoranylideneamino)quinolines **(4)** (1 equiv.), phenylboronic acid (1.2 equiv.), $Pd(PPh_3)_4$ (5% of **(4)**) and DMF (5 mL per mmol of **4**) were added to a two-necked flask equipped with a stirrer bar, rubber septum and a condenser. The mixture was flushed for 10 minutes with argon gas and then aqueous 2 *M* K_2CO_3 (2 mL per mmol of **(4)**) was added through a syringe. The mixture was degassed with argon for additional 10 minutes and a balloon filled with argon gas was connected to the top of the condenser. The stirred mixture was heated with stirring at 90 – 100°C under argon atmosphere for 48 hours and then allowed to cool to room temperature. The cooled mixture was poured into ice-cold water and the precipitate was collected by filtration and then recrystallized from ethanol to afford 2,3-diaryl-4-(triphenylphosphoranylideneamino)quinoline **(6)**.

2,3-Diphenyl-4-(triphenylphosphoranylideneamino)quinoline (6a). The compound was isolated as solid (75%) mp. 239 – 240°C (ethanol); ^{1}H nmr (300 MHz, $CDCl_3$): δ 6.75 (2H, d, *J* = 1.5 and 7.8 Hz), 6.95 – 7.12 (7H, m,), 7.18 – 7.34 (14H, m), 7.43 – 7.51 (4H, m), 7.81 (1H, d, *J* = 8.1 Hz), 8.03 (1H, d, *J* = 8.2 Hz); ^{13}C nmr (75 MHz, $CDCl_3$) δ: 123.8, 125.7, 125.8, 126.7, 126.8, 126.9, 127.2, 127.5, 128.3, 128.4 (d, $^3J_{CP}$ = 12.2 Hz), 129.3, 129.5, 131.5 (d, $^4J_{CP}$ = 2.9 Hz), 131.6 (d, $^1J_{CP}$ = 108.3 Hz), 132.0, 132.4 (d, $^2J_{CP}$ = 10.0 Hz), 140.5, 142.3, 148.5, 154.2, 159.8; ^{31}P nmr: δ 0,39; ir (neat): ν_{max}/cm^{-1} 748, 996, 1105, 1225, 1356, 1431, 1479, 1540, 3058; ms (EI) m/z 556 (M^+, 100), 295 (38), 262 (42), 183 (44); Hmrs (EI) calculated for $C_{39}H_{29}N_2P$: 556.2068. Found: 556.2051. *Anal. calc*. for $C_{39}H_{29}N_2P$: C, 84.22; H, 5.25; N, 5.04. Found: C, 83.97; H, 5.79; N, 5.44.

2-(4-Fluorophenyl)-3-phenyl-4-(triphenylphosphoranylideneamino)quinoline (6b). This compound was isolated as solid (85%) mp. 204 – 206°C (ethanol); ^{1}H nmr (300 MHz, $CDCl_3$): δ 6.72 – 6.81 (4H, m), 6.95 – 7.12 (5H, m), 7.17 – 7.34 (13H, m), 7.43 – 7.51 (4H, m), 7.79 (1H, d, *J* = 7.8 Hz), 8.01 (1H, d, *J* = 7.8 Hz); ^{13}C nmr (75 MHz, $CDCl_3$) δ: 114.1 (d, $^2J_{CF}$ = 21.1 Hz), 123.9, 125.7, 125.8, 126.7 (d, $^4J_{CP}$ = 2.9 Hz), 127.7, 128.4 (d, $^3J_{CP}$ = 12.5 Hz), 128.5, 129.1, 131.3 (d, $^2J_{CF}$ = 8.3 Hz), 131.4 (d, $^1J_{CP}$ = 103.9 Hz), 131.5 (d, $^4J_{CP}$ = 2.9 Hz), 131.9 (d, $^2J_{CP}$ = 10.2 Hz), 132.1, 132.4 (d, $^2J_{CP}$ = 9.9 Hz), 138.3 (d, $^1J_{CF}$ = 3.4 Hz), 140.3, 148.3, 154.5, 158.6, 161.8 (d, $^1J_{CF}$ = 244.1 Hz); ^{31}P nmr: δ 0.49; ir (neat): ν_{max}/cm^{-1} 714, 753, 994, 1108, 1223, 1434, 1481, 3056; ms (EI) m/z 574 (M^+, 100), 313 (72), 277 (40), 262 (51), 183 (57); Hmrs (EI) calculated for $C_{39}H_{28}N_2FP$: 574.1974. Found: 574.1986. *Anal. calc*. for $C_{39}H_{28}N_2FP$: C, 81.58; H, 4.91; N, 4.88. Found: C, 80.86; H, 4.98; N, 4.65.

2-(4-Chlorophenyl)-3-phenyl-4-(triphenylphosphoranylideneamino)quinoline (6c). This compound was isolated as solid (90%) mp. 235 – 236°C (ethanol); ^{1}H nmr (300 MHz, $CDCl_3$): δ 6.73 – 6.77 8 (2H, m), 6.96 – 7.13 (8H, m), 7.16 – 7.23 (6H, m), 7.27 – 7.34 (6H, m), 7.44 – 7.51 (4H, m), 7.79 (1H, dd, *J* = 0.6 and 8.1 Hz), 8.00 (1H, d, *J* = 7.8 Hz); ^{13}C nmr (75 MHz, $CDCl_3$) δ: 124.0, 125.8, 125.9, 126.8 (d, $^2J_{CP}$ = 2.9 Hz), 126.9, 127.4, 127.7, 128.4 (d, $^3J_{CP}$ = 12.5 Hz), 129.1, 129.2, 131.0, 131.4 (d, $^1J_{CP}$ = 103.8 Hz), 131.5 (d, $^4J_{CP}$ = 2.9 Hz), 131.9, 132.4 (d, $^2J_{CP}$ = 12.5 Hz), 132.7, 140.2, 140.7, 148.4, 154.5, 158.4, 162.5; ^{31}P nmr δ 0.50; ir (neat): ν_{max}/cm^{-1} 713, 756, 996, 1107, 1217, 1357, 1416, 1477, 1537, 3059; ms (EI) m/z 592 (58), 590 (M^+, 100), 262 (59), 183 (56); Hmrs (EI) calculated for $C_{39}H_{28}N_2{}^{35}ClP$: 590.1679. Found: 590.1694. *Anal. calc*. for $C_{39}H_{28}N_2{}^{35}ClP$: C, 79.37; H, 4.78; N, 4.75. Found: C, 78.98; H, 4.83; N, 4.59.

2-(4-Methoxyphenyl)-3-phenyl-4-(triphenylphosphoranylideneamino)quinoline (6d). This compound was isolated as solid (89%) mp. 242 – 244°C (ethanol); ^{1}H nmr (300 MHz, $CDCl_3$): δ 3.70 (3H, s), 6.34 (2H, d, *J* = 8.4 Hz), 6.77 (2H, d, *J* = 6.6 Hz), 6.96 (1H, t, *J* = 7.8 Hz), 7.01 – 7.09 (3H, m), 7.17 – 7.33 (14H, m), 7.43 – 7.49 (4H, m), 7.89 (1H, d, *J* = 8.4 Hz), 8.01 (1H, d, *J* 8.4 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 55.1, 112.7, 123.6, 125.6, 125.7, 126.7, 126.8, 127.6, 128.3, 128.4 (d, $^3J_{CP}$ = 12.5 Hz), 129.3, 130.9, 131.5 (d, $^4J_{CP}$ = 2.9 Hz), 131.6 (d, $^1J_{CP}$ = 102.2 Hz),

132.4 (d, $^2J_{CP}$ = 9.9 Hz), 135.0, 140.8, 148.5, 154.1, 158.9 (2 x C), 159.3; ^{31}P nmr: δ 0.15; ir (neat): ν_{max}/cm^{-1} 718, 1107, 1248, 1429, 1479, 3059; ms (EI) m/z 586 (M^+, 100), 368 (57), 325 (84), 236 (47), 97 (54), 69 (85); Hmrs (EI) calculated for $C_{40}H_{31}N_2OP$: 586.2174. Found: 586.2132. *Anal. calc*. for $C_{40}H_{31}N_2OP$: C, 81.95; H, 5.33; N, 4.78. Found: C, 81.85; H, 5.38; N, 4.26.

General Procedure for the Hydrolysis of (3) with Aqueous Acetic acid. A stirred solution of **(6)** (1 equiv.) in 80% acetic acid (5 mL per mmol of **(6)**) was boiled under reflux for 7 hours. Acetic acid was evaporated under reduced pressure and the residue was purified by column chromatography using ethyl acetate as eluent. The solvent was evaporated under reduced pressure and the solid residue washed with ice-cold methanol to remove excess triphenyl phosphine oxide to afford pure 4-amino-2,3-diarylquinoline **(7)**.

4-Amino-2,3-diphenylquinoline (7a). This compound was isolated as solid (80%) mp. 239 – 241°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.75 (2H, br s), 7.14 – 7.22 (5H, m), 7.26 – 7.37 (5H, m), 7.48 (1H, dt, *J* 0.9 and 7.6 Hz), 7.68 (1H, dt, *J* = 1.2 and 7.8 Hz), 7.79 (1H, dd, *J* = 0.6 and 8.4 Hz), 8.08 (1H, dd, *J* = 0.6 and 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 116.0, 117.4, 120.4, 125.0, 127.3, 127.4, 127.5, 129.0, 129.4, 129.7, 130.1, 131.1, 136.5, 141.2, 147.2, 147.5, 158.8; ir (neat): ν_{max}/cm^{-1} 760, 919, 940, 1305, 1362, 1423, 1493, 1562, 1635, 3087, 3298, 3437; ms (EI) m/z 296 (M^+, 81), 295 (100); Hmrs (EI) calculated for $C_{22}H_{16}N_2$: 296.1313. Found: 296.1313. *Anal. calc*. for $C_{22}H_{16}N_2$: C, 85.17; H, 5.33; N, 9.46. Found: C, 84.67; H, 5.33; N, 9.08.

4-Amino-2-(4-fluorophenyl)-3-phenylquinoline (7b). This compound was isolated as solid (75%), mp. 215 - 217°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.74 (2H, br s), 6.85 (2H, t, *J* = 8.7 Hz), 7.17 – 7.20 (2H, m), 7.26 – 7.38 (5H, m), 7.48 (1H, dt, *J* = 0.9 and 7.6 Hz), 7.68 (1H, dt, *J* = 1.2 and 7.8 Hz), 7.78 (1H, td, *J* = 0.6 and 8.1 Hz), 8.08 (1H, td, *J* = 1.2 and 7.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 114.5 (d, $^2J_{CF}$ = 21.4 Hz), 115.8, 117.4, 120.3, 125.1, 127.6, 129.1, 129.5, 130.1, 131.1, 131.4 (d, $^3J_{CF}$ = 8.3 Hz), 136.4, 137.3 (d, $^4J_{CF}$ = 3.5 Hz), 147.3, 147.5, 157.7, 162.2 (d, $^1J_{CF}$ = 245.0 Hz); ir (neat): ν_{max}/cm^{-1} 758, 838, 1221, 1397, 1494, 1569, 1603, 3058, 3429; ms (EI) m/z 314 (M^+, 61), 313 (100); Hmrs (EI) calculated for $C_{21}H_{15}N_2F$: 313.1201. Found: 313.1204. *Anal. calc*. for $C_{21}H_{15}N_2F$: C, 80.55; H, 4.83; N, 8.95. Found: C, 80.13; H, 4.68; N, 8.80.

4-Amino-2-(4-chlorophenyl)-3-phenylquinoline (7c). This compound was isolated as solid (65%), mp. 237 – 239°C; ^{1}H nmr (300 MHz, $CDCl_3$): δ 4.76 (2H, br s), 7.12 – 7.24 (4H, m), 7.24 – 7.38 (5H, m), 7.48 (1H, dt, *J* = 0.9 and 7.6 Hz), 7.69 (1H, dt, *J* = 1.2 and 7.8 Hz), 7.77 (1H, d, *J* = 8.1 Hz), 8.07 (1H, d, *J* = 8.7 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 115.7, 117.4, 120.4, 125.2, 127.6, 127.8, 129.2, 129.5, 130.1, 131.0, 131.1, 133.4, 136.2, 139.8, 147.4, 147.5, 157.4; ir (neat): ν_{max}/cm^{-1} 759, 829, 934, 1016, 1091, 1365, 1420, 1491, 1567, 1624, 3125, 3307, 3429; ms (EI) m/z 332 (50), 331 (65), 330 (M^+, 80), 329 (100); Hmrs (EI) calculated for $C_{21}H_{15}N_2{}^{35}Cl$: 330.0904. Found: 330.0903. *Anal. calc*. for $C_{22}H_{14}N_2{}^{35}Cl$: C, 76.41; H, 4.58; N, 8.49. Found: C, 76.17; H, 4.38; N, 8.40.

4-Amino-2-(4-methoxyphenyl)-3-phenylquinoline (7d). This compound was isolated as solid (90%) mp. 165 – 167°C; ^{1}H nmr (300 MHz, $CDCl_3$): δ 3.73 (3H, s), 4.71 (2H, br s), 6.69 (2H, d, *J* = 8.7 Hz), 7.19 – 7.38 (7H, m), 7.44 (1H, dt, *J* = 0.6 and 7.5 Hz), 7.66 (1H, dt, *J* = 0.9 and 7.6 Hz), 7.75 (1H, d, *J* = 8.4 Hz), 8.08 (1H, d, *J* = 8.7 Hz); ^{13}C nmr (75 MHz, $CDCl_3$): δ 55.1, 113.0, 115.9, 117.4, 120.4, 124.8, 127.4, 129.0, 129.3, 130.0, 131.1, 133.8, 136.8, 147.1, 147.6, 158.2, 158.9; ir (neat): ν_{max}/cm^{-1} 759, 829, 934, 1016, 1091, 1365, 1420, 1491, 1567, 1624, 3125, 3307, 3429; ms (EI) m/z 326 (M^+, 62), 325 (100), 282 (20); Hmrs (EI) calculated for $C_{22}H_{18}N_2O$: 326.1381. Found: 326.1381. *Anal. calc*. for $C_{22}H_{18}N_2O$: C, 81.02; H, 5.56; N, 8.59. Found: C, 80.91; H, 5.85; N, 8.57.

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