



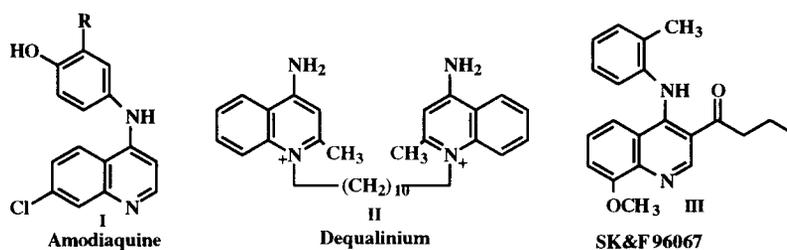
## An Efficient and General Method for the Synthesis of 3-Phosphorylated 4-Aminoquinolines from $\beta$ -Phosphine Oxide and Phosphonate Enamines.

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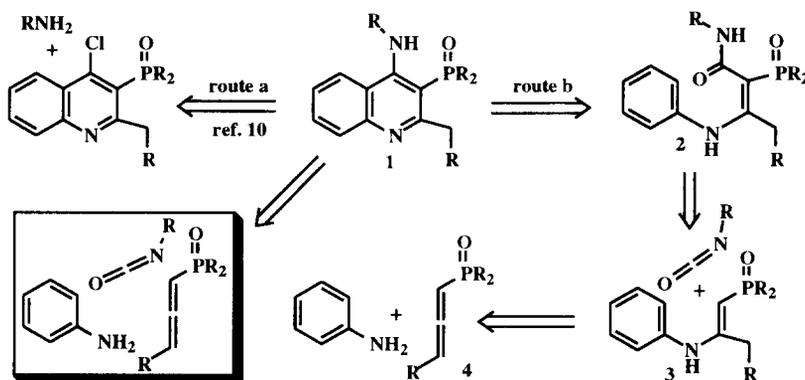
**Abstract:** An easy and efficient synthesis of 4-aminoquinolines substituted with a phosphine oxide **1**, phosphine sulphide **13** and phosphonate **11** group in the 3-position is described. The key step is a regioselective addition of lithiated  $\beta$ -enamino phosphine oxides **5** and phosphonate **6** to isocyanate and isothiocyanates to give functionalized amides **7**, **8** and thioamide **12**. Subsequent cyclization of these compounds with phosphorus oxychloride in the presence of triethylamine afforded the substituted 4-aminoquinolines **1**, **11** and **13**. © 1997 Elsevier Science Ltd. All rights reserved.

Quinoline ring systems represent an important class of compounds<sup>1</sup> and have attracted a great deal of attention in recent years because they constitute the backbone of a wide group of biologically active products such as alkaloids<sup>1,2a</sup> and azasteroids.<sup>2b</sup> Furthermore, the utility of 4-amino substituted quinolines has been recently demonstrated convincingly given that these compounds have interesting pharmacological properties and are widely used in medicinal chemistry. Amodiaquine **I** displays antimalarial activity,<sup>3</sup> while Dequalinium analogues **II** are potent and selective K<sup>+</sup> channel blockers.<sup>4</sup> 4-Arylaminoquinoline SK&F 96067 **III** has recently applied to the treatment of ulcers and related gastric disorders<sup>5</sup> (Scheme 1). Likewise, 4-aminoquinolines have been used as antiinflammatory<sup>6a</sup> and antihypertensive agents,<sup>6b</sup> as non-nucleoside HIV-1 inhibitors<sup>7</sup> and as reversible inhibitors of (H<sup>+</sup>/K<sup>+</sup>)-ATPase.<sup>5,8</sup> In these types of 4-aminoquinolines the presence of a carbonyl (see compound **III**, Scheme 1) or an ester group in the position 3 seems to play a key role in establishing the orientation of the arylamino group and therefore in the biological activity of these compounds.<sup>5,8</sup> With this in mind, we are interested in the design of new aminoquinoline derivatives substituted with a phosphine oxide, a phosphine sulphide or a phosphonate group in the 3 position of the heterocyclic system. These substituents could regulate important biological functions and could increase the biological activity of these type of compounds, in a similar way to that reported for other pharmaceuticals.<sup>9</sup> Furthermore, we assume that, in 4-aminoquinolines, the phosphoryl group, a phosphorus isosteric analogue of the carbonyl group, might be responsible for fixing the conformation about the 4-arylamino moiety through a combination of *intra* molecular hydrogen-bonding and  $\pi$ -electron delocalization.



Scheme 1

While there are many approaches available for quinoline derivatives,<sup>1a</sup> synthetic routes to 4-aminoquinolines are relatively few and most of them involve nucleophilic displacement of the chlorine atom of 4-chloroquinoline. **1a**,<sup>5,10</sup> (Scheme 2, *route a*) Likewise, 4-aminoquinolines can alternatively be prepared by tandem reactions that involve simultaneously both the construction of the quinoline ring and the introduction of the amino group in the position 4 (see Scheme 2, *route b*) such as been reported when functionalized amines,<sup>11a</sup> imines,<sup>11b,c</sup> enamines<sup>11d-h</sup> and carbodiimides<sup>11i,j</sup> have been used.



Scheme 2

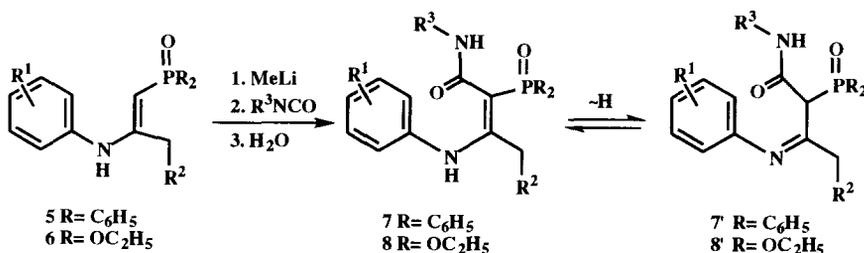
In connection with our interest in the synthesis of five<sup>12</sup> and six<sup>13</sup> membered phosphorylated nitrogen heterocycles we have used  $\beta$ -functionalized enamines derived from phosphazenes, phosphonium salts, phosphine oxides and phosphonates as synthetic intermediates in the synthesis of acyclic derivatives such as oximes<sup>14a</sup> allylamines,<sup>14b</sup> hydrazones,<sup>14c</sup> azadienes<sup>14d</sup> and aminodienes<sup>14e</sup> as well as phosphorus containing heterocycles.<sup>15</sup> In this context, we have recently described the synthesis of  $\beta$ -enamines derived from phosphine oxides and phosphonates and the use of these compounds as homologation reagents for the conversion of carbonyl derivatives into allylamines.<sup>16</sup> A recent publication,<sup>17</sup> reporting an excellent method for synthesis of aminoquinoline SK&F96067 (**III**, Scheme 1) has prompted us to report our own results concerning the preparation of 3-phosphorylated 4-aminoquinolines **1** from easily available starting material such as arylamines, isocyanates and phosphorylated allenes **4** (Scheme 2). Therefore, here we aim to extend the synthetic use of phosphorylated enamines **3** (R= Ph, OEt) in the preparation of substituted 4-aminoquinolines **1** containing phosphine oxide and phosphonate groups in the 3-position. Retrosynthetically,

we envisaged obtaining quinolines **1** by insertion of both a carbon atom and the amino group between the *ortho*-position of the aryl group and the enaminic carbon atom of functionalized compound **3** (Scheme 2). A tandem combination of isocyanates and phosphorus oxychloride was used and the key step in this synthetic methodology involved the regioselective reaction of metallated enamines **3** with isocyanates.

## RESULTS AND DISCUSSION

### Reaction of metallated enamines derived from phosphine oxides **5** and phosphonates **6** with isocyanates.

Enamines **5** ( $R^2 = H$ ), easily prepared by simple addition of amines to phosphine oxide allenes,<sup>16</sup> were treated with methyl lithium in tetrahydrofuran followed by addition of isocyanates (*TLC* control) and aqueous work-up giving polyfunctionalized phosphine oxides **7** in high yield (table 1, entries 1-7). Compounds **7** were characterized on the basis of their spectroscopic data, which indicate that they are isolated as the enamino tautomer **7**. Thus, the <sup>31</sup>P-NMR spectrum of **7a** showed absorption at  $\delta_P = 36.8$  ppm and in the <sup>1</sup>H-NMR spectrum of this derivative **7a** the methyl group gave a singlet at  $\delta_H = 1.48$ , and the enamine and imide protons resonates at  $\delta_H = 11.68$  and 13.72 ppm, while the <sup>13</sup>C-NMR spectrum showed absorptions at  $\delta_C = 83.3$  ( $^1J_{PC} = 115.8$  Hz) for the carbon bonded to phosphorus as well a doublet at 22.0 ppm ( $^3J_{PC} = 6.0$  Hz) assignable to the methyl group of the *E*-isomer.<sup>14b,c,16</sup>



Scheme 3

The substitution in the starting enamine **5** seems to play an important role in this process since when enamines **5** are substituted by an alkyl group ( $R^2 = \text{CH}_3$ ) a mixture of *Z* and *E* enamines **7** (table 1, entries 8,9) was obtained, whereas when enamines **5** are substituted by an aryl group ( $R^2 = p\text{-CH}_3\text{-C}_6\text{H}_4$ ) a mixture of not only *Z*- and *E*-enamines **7j** but also the  $\beta$ -iminophosphine oxide **7'j** was obtained (table 1, entry 10), although for our subsequent purposes the separation of the enamines and imines is not necessary. In <sup>1</sup>H-NMR the imine **7'j**, for example, showed clearly different absorptions related to the enamine tautomer **7j**, namely a doublet at  $\delta_H = 4.73$  ppm ( $^1J_{PC} = 15.4$  Hz) for the methine protons, and in the <sup>13</sup>C-NMR spectrum the methine carbon showed an absorption at  $\delta_C = 56.4$  ppm ( $^1J_{PC} = 51.1$  Hz), while in the <sup>13</sup>C-NMR spectrum of **7j** the absorption of the carbon bonded to phosphorus was shifted to lower field ( $\delta_C = 85.4$  and 95.9 ppm for *E*- and *Z*-isomers) relative to those of the imine compound **7'j**. Furthermore, in this case the <sup>31</sup>P-NMR spectrum of the mixture **7j/7'j** showed three different absorptions at  $\delta_P = 35.6$ , 35.0 and 31.5 ppm in an approximate isomer ratio 33/33/34 as evidenced by the relative peak areas for each compound, in

which the high-field chemical shift corresponds to the imine compound **7j**. Similarly, the enamine derived from phosphonate ester **6** reacted with phenylisocyanate and gave  $\beta$ -functionalized phosphonate **8** in very high yield (table 1, entry 11).

Table 1. Functionalized phosphine oxides **7/7'** and phosphonate **8** obtained.

Entry	Compound	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	Yield (%) <sup>a</sup>	Ratio(7:7') <sup>b</sup>	m.p. (°C)
1	<b>7a</b>	H	H	Ph	76	100 : 0	124-126
2	<b>7b</b>	<i>p</i> -Me	H	Ph	72	100 : 0	85-87
3	<b>7c</b>	<i>p</i> -MeO	H	Ph	83	100 : 0	77-80
4	<b>7d</b>	<i>o</i> -MeO	H	<i>o</i> -MePh	77	100 : 0	85-87
5	<b>7e</b>	3,4-(Me) <sub>2</sub>	H	Ph	74	100 : 0	86-88
6	<b>7f</b>	<i>o</i> -Br	H	Ph	71	100 : 0	85-88
7	<b>7g</b>	<i>m</i> -Cl	H	Ph	76	100 : 0	82-84
8	<b>7h</b>	H	Me	Ph	81	100 <sup>c</sup> : 0	130-132
9	<b>7i</b>	<i>p</i> -Me	Me	Ph	78	100 <sup>d</sup> : 0	168-170
10	<b>7j</b>	<i>p</i> -Me	<i>p</i> -MePh	Ph	72	66 <sup>e</sup> : 34	137-140
11	<b>8</b>	H	H	H	74	100 : 0	85-86

<sup>a</sup>Yield of isolated product **7/7'** and **8** based on **5**, **6**. <sup>b</sup>Enamino/imino and *Z/E* ratio determined by <sup>31</sup>P-NMR. <sup>c</sup>*Z/E* ratio (33/67). <sup>d</sup>*Z/E* ratio (32/68). <sup>e</sup>*Z/E* ratio (33/33).

#### Preparation of substituted 4-aminoquinolines from phosphine oxide **7** and phosphonate derivatives **8**.

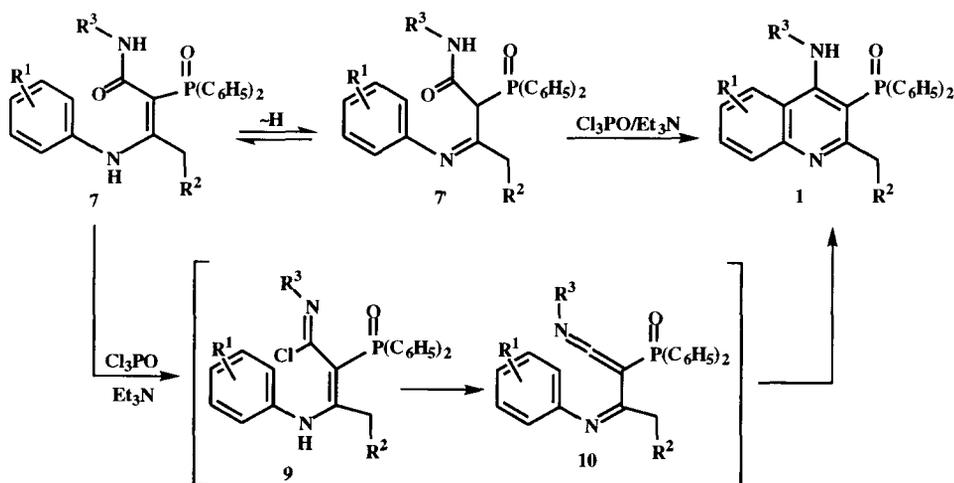
Treatment of functionalized enamines **7** with phosphorus oxychloride in the presence of triethylamine led to the formation of aminoquinolinylphosphine oxides **1** (Scheme 4) in excellent yield (table 2, entries 1-7). Spectroscopic data were in agreement with the assigned structure. Mass spectrometry of **1a** showed the molecular ion peak (*m/z* 434, 100 %), while the methyl group gave <sup>1</sup>H resonance at  $\delta_H = 2.04$  ppm. The formation of substituted quinolines **1** can be assumed to proceed *via* 6 $\pi$ -electrocyclization of conjugated imidoyl ketene imines **10** formed by the reaction of functionalized enamines **7** with phosphorus oxychloride in a similar way to that previously reported.<sup>11b,17</sup>

Formation of aminoquinolines were observed not only when enamines **7** were used, but also when a mixture of the *Z*- and *E*-enamines **7** and the imine-tautomers **7'** was used as starting material (Table 2, entries 8-10). The scope of this reaction was not limited to phosphine oxide derivatives **7**, since the enamine derived from phosphonate ester **8** also reacted with phosphorus oxychloride in the presence of triethylamine and gave in excellent yield the 4-aminoquinoline containing a phosphate group in 3 position **11** (Table 2, entry 11). From a preparative point of view it is noteworthy that the synthesis of phosphorylated 4-aminoquinolines **1** does not require the isolation and purification of functionalized phosphine oxides **7** and phosphonate **8** and they can be obtained in "one pot" reaction from the enamines derived from phosphine oxides **5** and phosphonate **6** when these compounds are directly metallated with methyl lithium in *THF* with subsequent addition of isocyanates phosphorus oxychloride and aqueous work-up.

Table 2. 4-Aminoquinolines **1**, **11** and **13** obtained.

Entry	Compound	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	Yield (%) <sup>a</sup>	m.p. (°C)
1	<b>1a</b>	H	H	Ph	78(67) <sup>b</sup>	188-190
2	<b>1b</b>	6-Me	H	Ph	72(62) <sup>b</sup>	218-220
3	<b>1c</b>	6-MeO	H	Ph	71	191-192
4	<b>1d</b>	8-MeO	H	<i>o</i> -MePh	74	197-199
5	<b>1e</b>	6,7-(Me) <sub>2</sub>	H	Ph	64	245-247
6	<b>1f</b>	8-Br	H	Ph	66	215-218
7	<b>1g</b>	7-Cl	H	Ph	69	207-208
8	<b>1h</b>	H	Me	Ph	76	169-171
9	<b>1i</b>	6-Me	Me	Ph	71	196-197
10	<b>1j</b>	6-Me	<i>p</i> -MePh	Ph	63	152-153
11	<b>11</b>	H	H	Ph	77 <sup>c</sup> (65) <sup>d</sup>	101-103
12	<b>13</b>	6-Me	H	Ph	72 <sup>e</sup>	152-155

<sup>a</sup> Yield of isolated product **1** based on **7**. <sup>b</sup>Yield of isolated product **1** in "one pot" reaction from **5**. <sup>c</sup>Yield of isolated product **11** based on **8**. <sup>d</sup>Yield of isolated product **11** in "one pot" reaction from **6**. <sup>e</sup>Yield of isolated product **13** based on **12**.



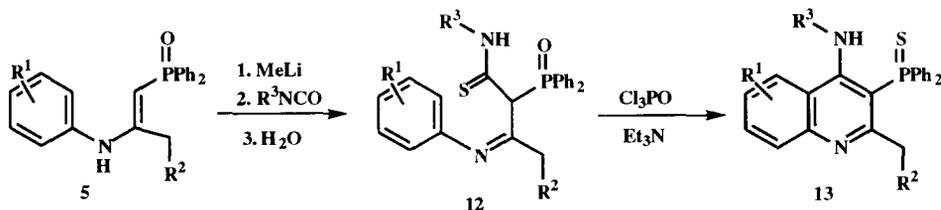
Scheme 4

#### Synthesis of 4-aminoquinolines derived from phosphine sulphides **13**.

This methodology used for the preparation of aminoquinolines **1** can also be applied to the synthesis of 4-aminoquinolines derived from phosphine sulphides **13** when isothiocyanates are used instead of isocyanates. Metallation of  $\beta$ -enamino phosphine oxides **5** with methyl lithium in tetrahydrofuran followed by addition of isothiocyanates (TLC control) and aqueous work-up afforded the functionalized thioamide **12**.

Treatment of thioamides **12** with phosphorus oxychloride in the presence of triethylamine gave aminoquinolinyl phosphine sulphides **13** (Scheme 5). Formation of these compounds **13** could be explained

by a similar process to that mentioned in Scheme 4, although with a spontaneous exchange of oxygen for sulphur, with transformation of phosphine oxide into the phosphine sulphide group, caused by the reaction conditions.



Scheme 5

In conclusion, we describe an easy and efficient method for synthesis of 4-aminoquinolines substituted with a phosphine oxide **1**, a phosphonate **11** and a phosphine sulphide **13** group in 3-position from readily available starting materials such as arylamines, allenes and isocyanates or isothiocyanates (see Scheme 2) and under mild reaction conditions. 4-Aminoquinolines are useful compounds in medicinal chemistry since these products display a broad range of biological activities and have been widely used as pharmaceuticals.<sup>3-8</sup>

#### ACKNOWLEDGEMENTS

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#### EXPERIMENTAL SECTION

**General.** Melting points were determined with a Buchi SPM-20 apparatus and are uncorrected. Analytical *TLC* was performed on 0.25mm silica gel plates (Merck). Visualization was accomplished by *UV* light and iodine. Solvents for extraction and chromatography were technical grade and distilled from the indicated drying agents: *CH*<sub>2</sub>*Cl*<sub>2</sub> (*P*<sub>2</sub>*O*<sub>5</sub>); *n*-hexane and diethyl ether (sodium benzophenone ketyl); ethyl acetate (*K*<sub>2</sub>*CO*<sub>3</sub>). All solvents used in reactions were freshly distilled from appropriate drying agents before use: acetonitrile (*P*<sub>2</sub>*O*<sub>5</sub>); *CHCl*<sub>3</sub> (*P*<sub>2</sub>*O*<sub>5</sub>). All other reagents were recrystallized or distilled as necessary. Column (flash) chromatography was carried out on silica gel (Merck, 70-230 mesh). Mass spectra were obtained on a Hewlett Packard 5890 spectrometer. Infrared spectra were taken on a Nicolet IRFT Magna 550 spectrometer. <sup>1</sup>*H-NMR* spectra were recorded on a Varian 300 MHz spectrometer using tetramethylsilane (0.00 ppm) or chloroform (7.26 ppm) as an internal reference in *CDCl*<sub>3</sub> solutions. <sup>13</sup>*C-NMR* spectra were recorded at 75 MHz with chloroform (77.0 ppm) as an internal reference in *CDCl*<sub>3</sub> solutions. <sup>31</sup>*P-NMR* spectra were recorded at 120 MHz with 85% phosphoric acid as an external reference. Elemental analyses were performed in a Perkin Elmer Model 240 instrument. Chemical shifts are given in ppm ( $\delta$ ); multiplicities are indicated by s (singlet), d (doublet), dd (double-doublet), t (triplet) q (quadruplet) or m (multiplet). Coupling constants, *J*, are reported in hertz. Infrared spectra (*IR*) were obtained as neat liquids, or as solids in *KBr*. Peaks are reported in cm<sup>-1</sup>. Mass spectra (*EI*) were obtained with a ionization voltage of 70 eV. Data are reported in the form *m/z* (intensity relative to base = 100). All reactions were performed in oven (125 °C) or flame-dried glassware under an inert atmosphere of dry *N*<sub>2</sub>.

**General procedure for the reaction of enamino carbanions derived from phosphine oxides **5** and phosphonate **6** with isocyanates or isothiocyanates.** A dry flask, 100-mL, 2-necked, fitted with a dropping funnel, gas inlet, and magnetic stirrer, was charged with 5 mmol of  $\beta$ -enamino phosphine oxides **5** and phosphonates **6** and 20 mL of *THF*. The temperature was allowed to descend to 0 °C and a solution (5.5 mmol) of methyl lithium in *THF* was then added. The mixture was allowed to stir for 1 h. A solution (5 mmol) of isocyanate or isothiocyanate in 10 mL of *THF* was added at this temperature. The mixture was stirred until *TLC* indicated the disappearance of the compound **5** or **6** (~ 16 h). The mixture was washed with water and extracted with *CH*<sub>2</sub>*Cl*<sub>2</sub>. The organic layers were dried over *MgSO*<sub>4</sub>, filtered and concentrated. The crude product was purified by recrystallization from diethyl ether.

**E-1-Phenylamide-2-(N-phenylamino)prop-1-enyldiphenylphosphine oxide (7a).** 1717 mg (76 %) of **7a** as a white solid. Data for **7a**: mp 124-126 °C;  $^1\text{H-NMR}$  (300 MHz) 1.48 (s, 3H, CH<sub>3</sub>), 6.93-7.83 (m, 20H, arom), 11.68 (s, 1H, NH), 13.72 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 22.0 (d,  $^3J_{\text{PC}} = 6.0$  Hz, CH<sub>3</sub>), 83.3 (d,  $^1J_{\text{PC}} = 115.8$  Hz, C-P), 118.7-138.8 (C-arom), 165.3 (d,  $^2J_{\text{PC}} = 17.1$  Hz), 170.2 (d,  $^2J_{\text{PC}} = 11.0$  Hz);  $^{31}\text{P-NMR}$  (120 MHz) 36.8; IR (KBr) 3254, 3053, 1602, 1548, 1490, 1132 cm<sup>-1</sup>; MS (EI) 452 (M<sup>+</sup>, 10). Anal. Calcd for C<sub>28</sub>H<sub>25</sub>N<sub>2</sub>O<sub>2</sub>P: C, 74.34; H, 5.53; N, 6.19. Found: C, 74.55; H, 5.38; N, 6.25.

**E-1-Phenylamide-2-(N-p-tolylamino)prop-1-enyldiphenylphosphine oxide (7b).** 1678 mg (72 %) of **7b** as a white solid. Data for **7b**: mp 85-87 °C;  $^1\text{H-NMR}$  (300 MHz) 1.52 (s, 3H, CH<sub>3</sub>), 2.31 (s, 3H, CH<sub>3</sub>), 6.93-7.87 (m, 19H, arom), 10.81 (s, 1H, NH), 12.95 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 20.9 (CH<sub>3</sub>), 22.1 (d,  $^3J_{\text{PC}} = 6.2$  Hz, CH<sub>3</sub>), 83.3 (d,  $^1J_{\text{PC}} = 116.3$  Hz, C-P), 120.9-139.0 (C-arom), 165.6 (d,  $^2J_{\text{PC}} = 16.9$  Hz), 170.4 (d,  $^2J_{\text{PC}} = 11.1$  Hz);  $^{31}\text{P-NMR}$  (120 MHz) 37.5; IR (KBr) 3433, 3059, 1542, 1439, 1223 cm<sup>-1</sup>; MS (EI) 466 (M<sup>+</sup>, 4). Anal. Calcd for C<sub>29</sub>H<sub>27</sub>N<sub>2</sub>O<sub>2</sub>P: C, 74.68; H, 5.79; N, 6.01. Found: C, 74.75; H, 5.68; N, 6.17.

**E-1-Phenylamide-2-(N-p-methoxyphenylamino)prop-1-enyldiphenylphosphine oxide (7c).** 2001 mg (83 %) of **7c** as a white solid. Data for **7c**: mp 78-80 °C;  $^1\text{H-NMR}$  (300 MHz) 1.42 (s, 3H, CH<sub>3</sub>), 3.71 (s, 3H, CH<sub>3</sub>), 6.75-7.82 (m, 19H, arom), 11.57 (s, 1H, NH), 13.46 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 21.9 (d,  $^3J_{\text{PC}} = 6.0$  Hz, CH<sub>3</sub>), 55.3 (O-CH<sub>3</sub>), 82.5 (d,  $^1J_{\text{PC}} = 116.7$  Hz, C-P), 114.2-158.0 (C-arom), 166.1 (d,  $^2J_{\text{PC}} = 17.6$  Hz), 170.3 (d,  $^2J_{\text{PC}} = 11.1$  Hz);  $^{31}\text{P-NMR}$  (120 MHz) 37.2; IR (KBr) 3191, 3054, 1540, 1510, 1247 cm<sup>-1</sup>; MS (EI) 482 (M<sup>+</sup>, 7). Anal. Calcd for C<sub>29</sub>H<sub>27</sub>N<sub>2</sub>O<sub>3</sub>P: C, 72.20; H, 5.60; N, 5.81. Found: C, 72.35; H, 5.69; N, 5.97.

**E-1-o-Tolylamide-2-(N-o-methoxyphenylamino)prop-1-enyldiphenylphosphine oxide (7d).** 1909 mg (77 %) of **7d** as a white solid. Data for **7d**: mp 85-87 °C;  $^1\text{H-NMR}$  (300 MHz) 1.42 (s, 3H, CH<sub>3</sub>), 2.01 (s, 3H, CH<sub>3</sub>), 3.77 (s, 3H, CH<sub>3</sub>), 6.75-7.82 (m, 18H, arom), 11.23 (s, 1H, NH), 13.45 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 17.2 (CH<sub>3</sub>), 21.5 (d,  $^3J_{\text{PC}} = 6.1$  Hz, CH<sub>3</sub>), 55.2 (O-CH<sub>3</sub>), 83.4 (d,  $^1J_{\text{PC}} = 116.6$  Hz, C-P), 110.2-158.0 (C-arom), 166.5 (d,  $^2J_{\text{PC}} = 17.7$  Hz), 170.4 (d,  $^2J_{\text{PC}} = 11.2$  Hz);  $^{31}\text{P-NMR}$  (120 MHz) 37.1; IR (KBr) 3189, 3050, 1533, 1521, 1235 cm<sup>-1</sup>; MS (EI) 496 (M<sup>+</sup>, 3). Anal. Calcd for C<sub>30</sub>H<sub>29</sub>N<sub>2</sub>O<sub>3</sub>P: C, 72.58; H, 5.85; N, 5.64. Found: C, 72.71; H, 5.73; N, 5.67.

**E-1-Phenylamide-2-(N-3,4-dimethylphenylamino)prop-1-enyldiphenylphosphine oxide (7e).** 1678 mg (74 %) of **7e** as a white solid. Data for **7e**: mp 86-87 °C;  $^1\text{H-NMR}$  (300 MHz) 1.46 (s, 3H, CH<sub>3</sub>), 2.14 (s, 6H, CH<sub>3</sub>), 6.76-7.80 (m, 18H, arom), 10.81 (s, 1H, NH), 12.95 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 19.2 (CH<sub>3</sub>), 19.7 (CH<sub>3</sub>), 22.0 (d,  $^3J_{\text{PC}} = 6.0$  Hz, CH<sub>3</sub>), 82.6 (d,  $^1J_{\text{PC}} = 116.8$  Hz, C-P), 118.8-138.9 (C-arom), 165.6 (d,  $^2J_{\text{PC}} = 17.1$  Hz), 170.4 (d,  $^2J_{\text{PC}} = 10.6$  Hz);  $^{31}\text{P-NMR}$  (120 MHz) 37.1; IR (KBr) 3052, 2952, 1542, 1441, 1320 cm<sup>-1</sup>; MS (EI) 480 (M<sup>+</sup>, 8). Anal. Calcd for C<sub>30</sub>H<sub>29</sub>N<sub>2</sub>O<sub>2</sub>P: C, 75.00; H, 6.04; N, 5.83. Found: C, 75.16; H, 6.08; N, 5.91.

**E-1-Phenylamide-2-(N-o-bromophenylamino)prop-1-enyldiphenylphosphine oxide (7f).** 1885 mg (71 %) of **7f** as a brown solid. Data for **7f**: mp 86-88 °C;  $^1\text{H-NMR}$  (300 MHz) 1.35 (s, 3H, CH<sub>3</sub>), 6.92-8.25 (m, 19H, arom), 11.62 (s, 1H, NH), 13.60 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 22.0 (d,  $^3J_{\text{PC}} = 6.0$  Hz, CH<sub>3</sub>), 84.6 (d,  $^1J_{\text{PC}} = 118.8$  Hz, C-P), 114.8-138.9 (C-arom), 165.0 (d,  $^2J_{\text{PC}} = 16.1$  Hz), 170.4 (d,  $^2J_{\text{PC}} = 10.6$  Hz);  $^{31}\text{P-NMR}$  (120 MHz) 37.3; IR (KBr) 3352, 3056, 1542, 1441, 1220 cm<sup>-1</sup>; MS (EI) 531 (M<sup>+</sup>-Br, 14). Anal. Calcd for C<sub>28</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub>PBr: C, 63.27; H, 4.52; N, 5.27. Found: C, 63.16; H, 4.38; N, 5.37.

**E-1-Phenylamide-2-(N-m-chlorophenylamino)prop-1-enyldiphenylphosphine oxide (7g).** 1847 mg (76 %) of **7g** as a brown solid. Data for **7g**: mp 82-84 °C;  $^1\text{H-NMR}$  (300 MHz) 1.51 (s, 3H, CH<sub>3</sub>), 6.62-7.83 (m, 19H, arom), 11.65 (s, 1H, NH), 13.79 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 21.9 (d,  $^3J_{\text{PC}} = 6.1$  Hz, CH<sub>3</sub>), 84.8 (d,  $^1J_{\text{PC}} = 119.0$  Hz, C-P), 114.7-139.3 (C-arom), 164.8 (d,  $^2J_{\text{PC}} = 16.1$  Hz), 170.0 (d,  $^2J_{\text{PC}} = 10.6$  Hz);  $^{31}\text{P-NMR}$  (120 MHz) 37.1; IR (KBr) 3341, 3066, 1595, 1555, 1441, 1220 cm<sup>-1</sup>; MS (EI) 486 (M<sup>+</sup>-Cl, 12). Anal. Calcd for C<sub>28</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub>PCl: C, 69.06; H, 4.93; N, 5.75. Found: C, 69.18; H, 4.78; N, 5.67.

**Z- and E-1-Phenylamide-2-(N-phenylamino)but-1-enyldiphenylphosphine oxide (7h).** 1887 mg (81 %) of **7h** as a white solid. Data for **7h**: mp 130-132 °C;  $^1\text{H-NMR}$  (300 MHz) 1.11 (m, 3H, E- and Z-CH<sub>3</sub>), 2.16 (m, 2H, E- and Z-CH<sub>2</sub>), 6.94-7.82 (m, 20H, arom), 11.66 (s, 1H, NH), 13.65 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 10.5 (CH<sub>3</sub>), 25.1 (d,  $^3J_{\text{PC}} = 9.5$  Hz, Z-CH<sub>2</sub>), 26.2 (d,  $^3J_{\text{PC}} = 6.1$  Hz, E-CH<sub>2</sub>), 82.8 (d,  $^1J_{\text{PC}} = 116.3$  Hz, E-C-P), 94.3 (d,  $^1J_{\text{PC}} = 102.1$  Hz, Z-C-P), 118.3-139.6 (C-arom), 167.3 (d,  $^2J_{\text{PC}} = 17.0$  Hz), 170.7 (d,  $^2J_{\text{PC}} = 12.7$  Hz);  $^{31}\text{P-NMR}$  (120 MHz) 35.1 and 36.6; IR (KBr) 3161, 1664, 1434, 1162 cm<sup>-1</sup>; MS (EI) 466 (M<sup>+</sup>, 4). Anal. Calcd for C<sub>29</sub>H<sub>27</sub>N<sub>2</sub>O<sub>2</sub>P: C, 74.68; H, 5.79; N, 6.01. Found: C, 74.82; H, 5.61; N, 5.88.

**Z- and E-1-Phenylamide-2-(N-p-tolylamino)but-1-enyldiphenylphosphine oxide (7i).** 1872 mg (78 %) of **7i** as a white solid. Data for **7i**: mp 168-170 °C;  $^1\text{H-NMR}$  (300 MHz) 1.07 (m, 3H, E- and Z-CH<sub>3</sub>), 2.11 (m, 2H, E- and Z-CH<sub>2</sub>), 2.24 (s, 3H, E- and Z-CH<sub>3</sub>), 6.91-7.87 (m, 19H, arom), 11.69 (s, 1H, NH), 13.35 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 10.3 (CH<sub>3</sub>), 20.9 (CH<sub>3</sub>), 25.2 (d,  $^3J_{\text{PC}} = 9.7$  Hz, Z-CH<sub>2</sub>), 26.0 (d,  $^3J_{\text{PC}} = 6.0$  Hz, E-CH<sub>2</sub>), 82.3 (d,  $^1J_{\text{PC}} = 116.8$  Hz, E-C-P), 94.7 (d,  $^1J_{\text{PC}} = 101.9$  Hz, Z-C-P), 119.1-139.7 (C-arom), 169.3 (d,  $^2J_{\text{PC}} = 17.1$  Hz), 171.2 (d,  $^2J_{\text{PC}} = 13.1$  Hz);  $^{31}\text{P-NMR}$  (120 MHz) 35.0 and 35.6; IR (KBr) 3161, 1664, 1434, 1162 cm<sup>-1</sup>; MS (EI) 480 (M<sup>+</sup>, 4). Anal. Calcd for C<sub>30</sub>H<sub>29</sub>N<sub>2</sub>O<sub>2</sub>P: C, 75.01; H, 6.04; N, 5.83. Found: C, 75.12; H, 6.11; N, 5.78.

**Z- and E-1-Phenylamide-2-(N-p-tolylamino)-3-p-tolylprop-1-enyldiphenylphosphine oxide (7j) and 1-Phenylamide-2-(N-p-tolylimino)-3-p-tolylpropyldiphenylphosphine oxide (7j').** 2001 mg (72 %) of **7j/7j'** as a white solid. Data for **7j/7j'**: mp

138–139 °C;  $^1\text{H-NMR}$  (300 MHz)  $\delta$ : 2.10 (s, 3H, *E*- and *Z*-CH<sub>3</sub>), 2.15 (s, 3H, *E*- and *Z*-CH<sub>3</sub>), 3.38 (s, 2H, *E*- and *Z*-CH<sub>2</sub>), 6.17–7.93 (m, 23H, arom), 11.59 (s, 1H, NH), 13.21 (s, 1H, NH).  $\delta$ : 2.18 (s, 3H, CH<sub>3</sub>), 2.25 (s, 3H, CH<sub>3</sub>), 3.87 (s, 2H, CH<sub>2</sub>), 4.73 (d,  $^2J_{\text{PH}} = 15.4$  Hz, CH-P), 6.17–7.93 (m, 23H, arom), 10.27 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz)  $\delta$ : 20.7 (CH<sub>3</sub>), 20.8 (CH<sub>3</sub>), 35.8 (d,  $^3J_{\text{PC}} = 9.0$  Hz, *Z*-CH<sub>2</sub>), 37.6 (d,  $^3J_{\text{PC}} = 6.0$  Hz, *E*-CH<sub>2</sub>), 85.4 (d,  $^1J_{\text{PC}} = 115.2$  Hz, *E*-C-P), 95.9 (d,  $^1J_{\text{PC}} = 102.2$  Hz, *Z*-C-P), 119.1–138.7 (C-arom), 165.7 (d,  $^2J_{\text{PC}} = 13.1$  Hz), 166.7 (d,  $^2J_{\text{PC}} = 7.0$  Hz), 167.1 (d,  $^2J_{\text{PC}} = 17.1$  Hz), 170.4 (d,  $^2J_{\text{PC}} = 11.5$  Hz).  $\delta$ : 20.7 (CH<sub>3</sub>), 20.8 (CH<sub>3</sub>), 56.4 (d,  $^1J_{\text{PC}} = 51.1$  Hz, C-P), 119.1–138.7 (C-arom), 162.5 (d,  $^2J_{\text{PC}} = 2.5$  Hz), 162.8 (d,  $^2J_{\text{PC}} = 2.0$  Hz);  $^{31}\text{P-NMR}$  (120 MHz)  $\delta$ : 35.0 and 35.6.  $\delta$ : 31.5; IR (KBr) 3161, 1664, 1434, 1162 cm<sup>-1</sup>; MS (EI) 480 (M<sup>+</sup>, 4). Anal. Calcd for C<sub>30</sub>H<sub>29</sub>N<sub>2</sub>O<sub>2</sub>P: C, 75.01; H, 6.04; N, 5.83. Found: C, 75.12; H, 6.11; N, 5.78.

***E*-1-Phenylamide-2-(*N*-phenylamino)prop-1-enyldiethylphosphonate (8)**, 861 mg (74 %) of **8** as a white solid. Data for **8**: mp 85–86 °C;  $^1\text{H-NMR}$  (300 MHz) 1.28 (t, 6H,  $^3J_{\text{HH}} = 7.0$  Hz, CH<sub>3</sub>), 2.18 (s, 3H, CH<sub>3</sub>), 4.09 (m, 4H, CH<sub>2</sub>), 6.94–7.53 (m, 10H, arom), 11.38 (s, 1H, NH), 12.65 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 16.0 and 16.2 (CH<sub>3</sub>), 19.2 (d,  $^3J_{\text{PC}} = 3.1$  Hz, CH<sub>3</sub>), 81.7 (d,  $^1J_{\text{PC}} = 196.4$  Hz, C-P), 119.1–138.9 (C-arom), 168.8 (d,  $^2J_{\text{PC}} = 16.1$  Hz), 169.5 (d,  $^2J_{\text{PC}} = 19.7$  Hz);  $^{31}\text{P-NMR}$  (120 MHz) 27.3; IR (KBr) 3200, 2986, 1542, 1333 cm<sup>-1</sup>; MS (EI) 388 (M<sup>+</sup>, 10). Anal. Calcd for C<sub>20</sub>H<sub>25</sub>N<sub>2</sub>O<sub>4</sub>P: C, 61.86; H, 6.43; N, 7.22. Found: C, 61.98; H, 6.38; N, 7.25.

**1-Phenylthioamide-2-(*N*-*p*-tolylimino)propyldiphenylphosphine oxide (12)**, 1996 mg (83 %) of **12** as a yellow solid. Data for **12**: mp 145–146 °C;  $^1\text{H-NMR}$  (300 MHz) 1.78 (s, 3H, CH<sub>3</sub>), 2.11 (s, 3H, CH<sub>3</sub>), 5.30 (d,  $^2J_{\text{PH}} = 9.1$  Hz, CH-P), 6.36–7.94 (m, 19H, arom), 10.51 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 20.8 (CH<sub>3</sub>), 22.5 (CH<sub>3</sub>), 68.2 (d,  $^1J_{\text{PC}} = 47.3$  Hz, C-P), 119.3–138.9 (C-arom), 165.5 (C=N), 189.1 (C=S);  $^{31}\text{P-NMR}$  (120 MHz) 30.3; IR (KBr) 3174, 3005, 1592, 1513, 1373, 1149 cm<sup>-1</sup>; MS (EI) 482 (M<sup>+</sup>, 17). Anal. Calcd for C<sub>29</sub>H<sub>27</sub>N<sub>2</sub>O<sub>2</sub>SP: C, 72.21; H, 5.60; N, 5.81. Found: C, 72.45; H, 5.48; N, 5.75.

**General procedure for the preparation of the phosphorylated quinolines 1, 11 and 13.** A dry flask, 100-mL, 2-necked, fitted with a dropping funnel, gas inlet, and magnetic stirrer, was charged with (3 mmol) of amide **7**, **8** or thioamide **12**, 0.55 mL (4 mmol) of triethylamine and 15 mL of THF. A solution 0.30 mL (3.2 mmol) of phosphorus oxychloride and 10 mL of THF was added over 10 min. The mixture was stirred and refluxed until TLC indicated the disappearance of the compound **7**, **8** or **12** (–2 days). The mixture was diluted with 30 mL water and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 15). The CH<sub>2</sub>Cl<sub>2</sub> layers were washed with water. The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated. The crude product was purified by flash-chromatography on silica gel (hexane/diethyl ether, 1/1). Quinolines can also be obtained in "one pot" reaction: 4 mmol of **5** in 20 mL of THF was metallated with methyl lithium at 0 °C. The mixture was allowed to stir for 1 h. A solution 4 mmol of isocyanate in 10 mL of THF was added at this temperature. The mixture was stirred for 24 h, and a solution of 0.39 mL (4.2 mmol) of phosphorus oxychloride and 10 mL of THF was added. The quinoline was purified as described above.

**3-Diphenylphosphoryl-2-methyl-4-phenylaminoquinoline (1a)**, 1015 mg (78 %) of **1a** as a yellow solid. Data for **1a**: mp 188–190 °C;  $^1\text{H-NMR}$  (300 MHz) 2.04 (s, 3H, CH<sub>3</sub>), 7.04–7.80 (m, 19H, arom), 10.96 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 28.4 (CH<sub>3</sub>), 106.7 (d,  $^1J_{\text{PC}} = 98.2$  Hz, C-P), 119.9–158.4 (C-arom);  $^{31}\text{P-NMR}$  (120 MHz) 38.7; IR (KBr) 3200, 3059, 1568, 1400, 1118 cm<sup>-1</sup>; MS (EI) 434 (M<sup>+</sup>, 100). Anal. Calcd for C<sub>28</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub>P: C, 77.42; H, 5.30; N, 6.45. Found: C, 77.61; H, 5.53; N, 6.55.

**3-Diphenylphosphoryl-2,6-dimethyl-4-phenylaminoquinoline (1b)**, 968 mg (72 %) of **1b** as a yellow solid. Data for **1b**: mp 218–220 °C;  $^1\text{H-NMR}$  (300 MHz) 2.02 (s, 3H, CH<sub>3</sub>-C=N), 2.18 (s, 3H, CH<sub>3</sub>), 6.70–7.73 (m, 18H, arom), 10.84 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 21.9 (CH<sub>3</sub>), 28.2 (CH<sub>3</sub>), 107.0 (d,  $^1J_{\text{PC}} = 99.1$  Hz, C-P), 120.1–157.7 (C-arom);  $^{31}\text{P-NMR}$  (120 MHz) 38.2; IR (KBr) 3261, 3059, 1609, 1575, 1179 cm<sup>-1</sup>; MS (EI) 448 (M<sup>+</sup>, 88). Anal. Calcd for C<sub>29</sub>H<sub>25</sub>N<sub>2</sub>O<sub>2</sub>P: C, 77.68; H, 5.58; N, 6.25. Found: C, 77.51; H, 5.69; N, 6.51.

**3-Diphenylphosphoryl-2-methyl-6-methoxy-4-phenylaminoquinoline (1c)**, 988 mg (71 %) of **1c** as a yellow solid. Data for **1c**: mp 191–192 °C;  $^1\text{H-NMR}$  (300 MHz) 2.01 (s, 3H, CH<sub>3</sub>-C=N), 3.33 (s, 3H, CH<sub>3</sub>-O), 6.72–7.73 (m, 18H, arom), 10.82 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 28.0 (CH<sub>3</sub>), 54.8 (CH<sub>3</sub>-O), 107.3 (d,  $^1J_{\text{PC}} = 98.2$  Hz, C-P), 104.7–156.9 (C-arom);  $^{31}\text{P-NMR}$  (120 MHz) 38.6; IR (KBr) 3113, 3027, 1568, 1491, 1238 cm<sup>-1</sup>; MS (EI) 464 (M<sup>+</sup>, 88). Anal. Calcd for C<sub>29</sub>H<sub>25</sub>N<sub>2</sub>O<sub>2</sub>P: C, 75.01; H, 5.39; N, 6.03. Found: C, 75.23; H, 5.54; N, 6.11.

**3-Diphenylphosphoryl-2-methyl-8-methoxy-4-*o*-tolylaminoquinoline (1d)**, 1061 mg (74 %) of **1d** as a yellow solid. Data for **1d**: mp 197–199 °C;  $^1\text{H-NMR}$  (300 MHz) 2.02 (s, 3H, CH<sub>3</sub>-C=N), 2.16 (s, 3H, CH<sub>3</sub>), 3.37 (s, 3H, CH<sub>3</sub>-O), 6.69–7.63 (m, 17H, arom), 10.67 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 25.4 (CH<sub>3</sub>), 28.0 (CH<sub>3</sub>), 54.6 (CH<sub>3</sub>-O), 106.9 (d,  $^1J_{\text{PC}} = 98.0$  Hz, C-P), 104.3–157.5 (C-arom);  $^{31}\text{P-NMR}$  (120 MHz) 38.5; IR (KBr) 3121, 3019, 1561, 1482, 1223 cm<sup>-1</sup>; MS (EI) 478 (M<sup>+</sup>, 88). Anal. Calcd for C<sub>30</sub>H<sub>27</sub>N<sub>2</sub>O<sub>2</sub>P: C, 75.31; H, 5.65; N, 5.86. Found: C, 75.43; H, 5.52; N, 5.91.

**3-Diphenylphosphoryl-2,6,7-trimethyl-4-phenylaminoquinoline (1e)**, 887 mg (64 %) of **1e** as a yellow solid. Data for **1e**: mp 245–247 °C;  $^1\text{H-NMR}$  (300 MHz) 2.04 (s, 3H, CH<sub>3</sub>-C=N), 2.11 (s, 3H, CH<sub>3</sub>), 2.36 (s, 3H, CH<sub>3</sub>), 6.74–7.75 (m, 17H, arom), 10.84 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 19.9 (CH<sub>3</sub>), 20.2 (CH<sub>3</sub>), 28.2 (CH<sub>3</sub>), 106.1 (d,  $^1J_{\text{PC}} = 99.7$  Hz, C-P), 118.3–157.4 (C-arom);  $^{31}\text{P-NMR}$  (120 MHz) 38.4; IR (KBr) 3269, 2978, 1712, 1594, 1430, 1115 cm<sup>-1</sup>; MS (EI) 462 (M<sup>+</sup>, 95). Anal. Calcd for C<sub>30</sub>H<sub>27</sub>N<sub>2</sub>O<sub>2</sub>P: C, 77.92; H, 5.84; N, 6.06. Found: C, 77.71; H, 5.72; N, 6.14.

**8-bromo-3-Diphenylphosphoryl-2-methyl-4-phenylaminoquinoline (1f)**, 1016 mg (66 %) of **1f** as a yellow solid. Data for **1f**: mp 215–218 °C;  $^1\text{H-NMR}$  (300 MHz) 2.09 (s, 3H, CH<sub>3</sub>), 6.71–7.90 (m, 18H, arom), 11.03 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75

MHz) 27.6 (CH<sub>3</sub>), 107.4 (d, <sup>1</sup>J<sub>PC</sub> = 98.6 Hz, C-P), 117.2-152.2 (C-arom); <sup>31</sup>P-NMR (120 MHz) 38.8; IR (KBr) 3341, 3294, 1649, 1552, 1238 cm<sup>-1</sup>; MS (EI) 513 (M<sup>+</sup>, 98). Anal. Calcd for C<sub>28</sub>H<sub>22</sub>N<sub>2</sub>OPBr: C, 65.50; H, 4.29; N, 5.46. Found: C, 65.61; H, 4.33; N, 5.35.

**7-chloro-3-Diphenylphosphoryl-2-methyl-4-phenylaminoquinoline (1g).** 969 mg (69 %) of **1g** as a yellow solid. Data for **1g**: mp 207-208 °C; <sup>1</sup>H-NMR (300 MHz) 2.11 (s, 3H, CH<sub>3</sub>), 6.77-7.94 (m, 18H, arom), 10.95 (s, 1H, NH); <sup>13</sup>C-NMR (75 MHz) 26.6 (CH<sub>3</sub>), 106.5 (d, <sup>1</sup>J<sub>PC</sub> = 99.1 Hz, C-P), 116.5-152.9 (C-arom); <sup>31</sup>P-NMR (120 MHz) 39.1; IR (KBr) 3365, 3094, 1633, 1542, 1211 cm<sup>-1</sup>; Anal. Calcd for C<sub>28</sub>H<sub>22</sub>N<sub>2</sub>OPCl: C, 71.79; H, 4.70; N, 5.98. Found: C, 71.90; H, 4.63; N, 5.85.

**3-Diphenylphosphoryl-2-ethyl-4-phenylaminoquinoline (1h).** 1021 mg (76 %) of **1h** as a yellow solid. Data for **1h**: mp 169-171 °C; <sup>1</sup>H-NMR (300 MHz) 0.58 (t, 3H, <sup>3</sup>J<sub>HH</sub> = 7.2 Hz, CH<sub>3</sub>), 2.40 (q, 2H, <sup>3</sup>J<sub>HH</sub> = 7.2 Hz, CH<sub>2</sub>), 6.75-7.98 (m, 19H, arom), 11.05 (s, 1H, NH); <sup>13</sup>C-NMR (75 MHz) 12.8 (CH<sub>3</sub>), 32.9 (CH<sub>2</sub>), 105.7 (d, <sup>1</sup>J<sub>PC</sub> = 99.7 Hz, C-P), 119.0-163.2 (C-arom); <sup>31</sup>P-NMR (120 MHz) 39.7; IR (KBr) 3335, 3056, 1602, 1568, 1407, 1125 cm<sup>-1</sup>; MS (EI) 448 (M<sup>+</sup>, 97). Anal. Calcd for C<sub>29</sub>H<sub>25</sub>N<sub>2</sub>OP: C, 77.68; H, 5.58; N, 6.25. Found: C, 77.78; H, 5.73; N, 6.20.

**3-Diphenylphosphoryl-2-methyl-4-phenylaminoquinoline (1i).** 984 mg (71 %) of **1i** as a yellow solid. Data for **1i**: mp 196-197 °C; <sup>1</sup>H-NMR (300 MHz) 0.57 (t, 3H, <sup>3</sup>J<sub>HH</sub> = 7.3 Hz, CH<sub>3</sub>), 2.19 (s, 3H, CH<sub>3</sub>), 2.38 (q, 2H, <sup>3</sup>J<sub>HH</sub> = 7.3 Hz, CH<sub>2</sub>), 6.72-7.75 (m, 18H, arom), 11.00 (s, 1H, NH); <sup>13</sup>C-NMR (75 MHz) 12.9 (CH<sub>3</sub>), 21.6 (CH<sub>3</sub>), 32.8 (CH<sub>2</sub>), 106.0 (d, <sup>1</sup>J<sub>PC</sub> = 99.2 Hz, C-P), 119.8-162.2 (C-arom); <sup>31</sup>P-NMR (120 MHz) 38.7; IR (KBr) 3046, 2989, 1593, 1414, 1114 cm<sup>-1</sup>; MS (EI) 462 (M<sup>+</sup>, 100). Anal. Calcd for C<sub>30</sub>H<sub>27</sub>N<sub>2</sub>OP: C, 77.92; H, 5.84; N, 6.06. Found: C, 77.75; H, 5.76; N, 6.21.

**3-Diphenylphosphoryl-2-(p-tolylmethyl)-6-methyl-4-phenylaminoquinoline (1j).** 1017 mg (63 %) of **1j** as a yellow solid. Data for **1j**: mp 152-153 °C; <sup>1</sup>H-NMR (300 MHz) 1.27 (t, 6H, <sup>3</sup>J<sub>HH</sub> = 6.9 Hz, CH<sub>3</sub>), 2.30 (s, 3H, CH<sub>3</sub>), 3.92 (s, 2H, CH<sub>2</sub>), 6.48-7.86 (m, 22H, arom), 10.76 (s, 1H, NH); <sup>13</sup>C-NMR (75 MHz) 20.8 (CH<sub>3</sub>), 21.6 (CH<sub>3</sub>), 43.8 (CH<sub>2</sub>), 108.8 (d, <sup>1</sup>J<sub>PC</sub> = 97.7 Hz, C-P), 108.0-158.8 (C-arom); <sup>31</sup>P-NMR (120 MHz) 37.6; IR (KBr) 3205, 3063, 1693, 1487, 1412 cm<sup>-1</sup>; MS (EI) 538 (M<sup>+</sup>, 100). Anal. Calcd for C<sub>36</sub>H<sub>31</sub>N<sub>2</sub>OP: C, 80.30; H, 5.76; N, 5.20. Found: C, 80.15; H, 5.66; N, 5.31.

**3-Diethylphosphonate-2-methyl-4-phenylaminoquinoline (1k).** 855 mg (77 %) of **1k** as a yellow solid. Data for **1k**: mp 101-103 °C; <sup>1</sup>H-NMR (300 MHz) 1.27 (t, 6H, <sup>3</sup>J<sub>HH</sub> = 6.9 Hz, CH<sub>3</sub>), 2.78 (s, 3H, CH<sub>3</sub>), 3.97-4.10 (m, 4H, CH<sub>2</sub>), 6.82-7.83 (m, 9H, arom), 10.39 (s, 1H, NH); <sup>13</sup>C-NMR (75 MHz) 16.1 (CH<sub>3</sub>), 26.3 (CH<sub>3</sub>), 62.3 (CH<sub>2</sub>), 103.9 (d, <sup>1</sup>J<sub>PC</sub> = 178.8 Hz, C-P), 119.4-160.1 (C-arom); <sup>31</sup>P-NMR (120 MHz) 22.4; IR (KBr) 3241, 2985, 1602, 1488, 1407, 1031 cm<sup>-1</sup>; MS (EI) 370 (M<sup>+</sup>, 100). Anal. Calcd for C<sub>20</sub>H<sub>23</sub>N<sub>2</sub>O<sub>3</sub>P: C, 64.86; H, 6.21; N, 7.57. Found: C, 64.78; H, 6.13; N, 7.70.

**3-Diphenylthiophosphoryl-2,6-dimethyl-4-phenylaminoquinoline (1l).** 1002 mg (72 %) of **1l** as a yellow solid. Data for **1l**: mp 152-155 °C; <sup>1</sup>H-NMR (300 MHz) 2.05 (s, 3H, CH<sub>3</sub>-C=N), 2.19 (s, 3H, CH<sub>3</sub>), 6.28-7.87 (m, 18H, arom), 8.44 (s, 1H, NH); <sup>13</sup>C-NMR (75 MHz) 21.5 (CH<sub>3</sub>), 27.8 (CH<sub>3</sub>), 107.0 (d, <sup>1</sup>J<sub>PC</sub> = 99.1 Hz, C-P), 116.8-158.4 (C-arom); <sup>31</sup>P-NMR (120 MHz) 35.9; IR (KBr) 3194, 3052, 1715, 1501, 1441, 1098 cm<sup>-1</sup>; MS (EI) 464 (M<sup>+</sup>, 100). Anal. Calcd for C<sub>29</sub>H<sub>25</sub>N<sub>2</sub>SP: C, 75.00; H, 5.38; N, 6.03. Found: C, 75.11; H, 5.59; N, 5.91.

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