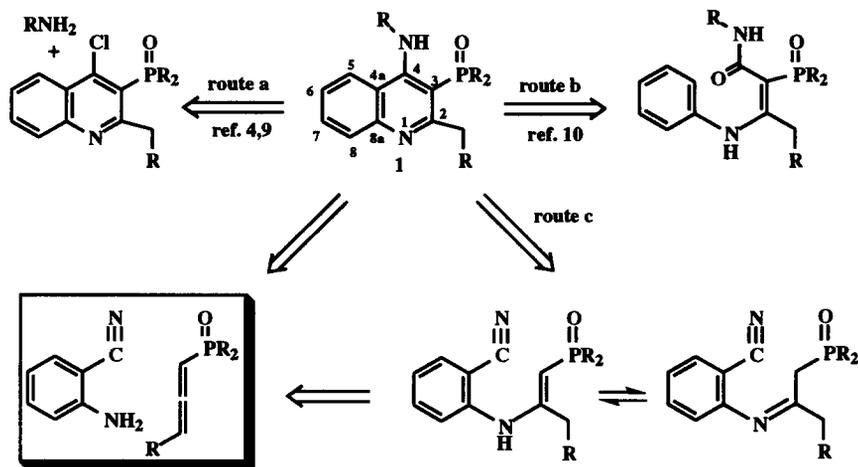




While there are many approaches available for quinoline derivatives,<sup>8</sup> synthetic routes to 4-aminoquinolines **1** are relatively few and most of them involve nucleophilic displacement of the chlorine atom of 4-chloroquinoline<sup>1,4,9</sup> (Scheme 2, *route a*). Alternatively, 4-aminoquinolines can be prepared by tandem reactions that involve simultaneous construction of the quinoline ring<sup>1</sup> (carbon-carbon bond formation, C<sub>4</sub>-C<sub>4a</sub>) and introduction of the amino group in the position 4 (Scheme 2, *route b*), as has been recently reported when functionalized  $\beta$ -enamines have been used.<sup>10</sup>



Scheme 2

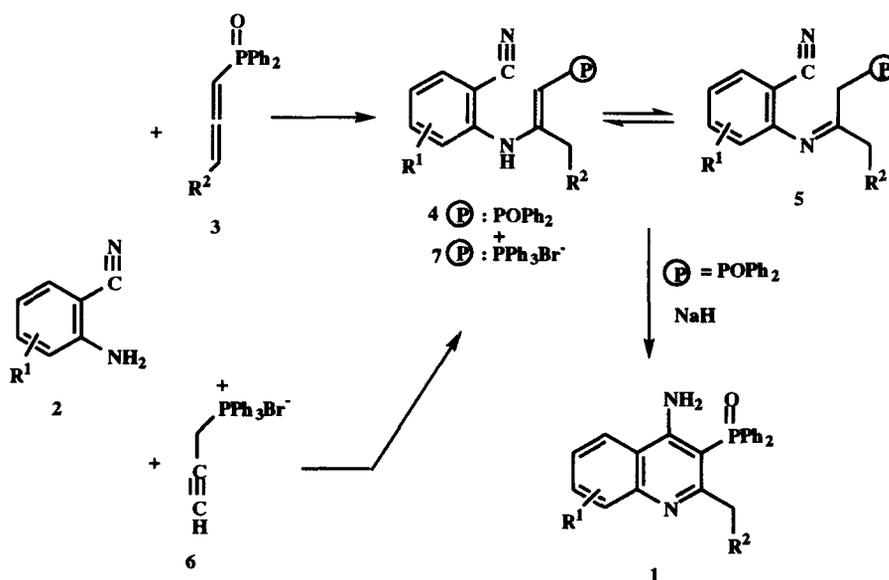
In connection with our interest in the chemistry of phosphazenes<sup>11,12</sup> and phosphorylated enamines we have used these compounds as synthetic intermediates for the preparation of heterocycles.<sup>13</sup> In this context, we have recently described the synthesis of *N*-aryl-4-aminoquinolines<sup>10</sup> from functionalized  $\beta$ -enamines derived from phosphine oxides and phosphonates (Scheme 2, *route b*). Here we aim to extend the synthetic use of phosphorylated enamines in the preparation of substituted 4-aminoquinolines **1** containing the phosphine oxide group in the 3-position. Retrosynthetically, we envisaged obtaining quinolines **1** by heterocyclization processes involving carbon-carbon bond formation (C<sub>3</sub>-C<sub>4</sub>) of functionalized imines or enamines containing a cyano group in the *ortho*-position of the aryl group (Scheme 2, *route c*) and that these key intermediates could be prepared by simple addition of *o*-aminobenzonitrile to allenes derived from phosphine oxides in a similar way to that reported for other amino compounds.<sup>14</sup>

## RESULTS AND DISCUSSION

### Synthesis of 3-phosphorylated 4-aminoquinolines **1**.

The preparation of phosphine oxide derivatives containing a cyano group **4/5** was accomplished easily and in high yields by means of addition of substituted *o*-aminobenzonitriles **2** to phosphine oxide allenes<sup>15</sup> **3** in refluxing acetonitrile (Table 1). Compounds **4/5** were characterized by their spectroscopic data, which indicated that they are isolated as a mixture of *Z*- and *E*- $\beta$ -enamino compounds **4** (minor products) and the  $\beta$ -

iminophosphine oxides **5** (major compounds), although for our purposes the separation of enamines and imines is not necessary for subsequent reactions. Thus, the  $^{31}\text{P-NMR}$  spectrum for crude compound **4/5a** showed three different absorptions at  $\delta_{\text{P}}$  25.6, 28.8 and 29.7 ppm in an approximate isomer ratio 5 : 85 : 10 as evidenced by the relative peak areas for each compound, in which the high-field and the low-field chemical shift corresponds to the *E*-isomer and the *Z*-isomer **4a**. In the  $^1\text{H-NMR}$  spectrum of **4a**, the vinylic proton resonates at  $\delta_{\text{H}}$  5.02 ppm as a well resolved doublet with coupling constant of  $^2J_{\text{PH}} = 17.7$  Hz, and the methyl group gives a singlet at  $\delta_{\text{H}}$  2.03 ppm, while the  $^{13}\text{C-NMR}$  shows absorptions at  $\delta_{\text{C}}$  81.0 ppm ( $^1J_{\text{PC}} = 128.8$  Hz) and 23.2 ppm ( $^3J_{\text{PC}} = 5.4$  Hz) assignable to the carbon bonded to phosphorus and the methyl group of the *E*-isomer.<sup>16</sup> Conversely, for **4a** the *Z*-isomer showed clearly different absorptions, namely a doublet at  $\delta_{\text{H}}$  4.18 ppm ( $^2J_{\text{PC}} = 22.2$  Hz) for the vinylic proton as well as a low-field signal for the methyl group at  $\delta_{\text{H}}$  2.19 ppm, while in the  $^{13}\text{C-NMR}$  spectrum the absorption of methine carbon is shifted to higher field ( $\delta_{\text{C}}$  77.2 ppm) with a lower value of the phosphorus-carbon coupling constant ( $^1J_{\text{PC}} = 114.2$  Hz) relative to those of the *E*-isomer. Vicinal  $^{13}\text{C}$ - $^{31}\text{P}$  coupling constant ( $^3J_{\text{PC}} = 14.7$  Hz) showed that the methyl group and phosphorus atom in the  $\beta$ -enamino compound **4a** are *trans* related.<sup>16</sup> On the other hand, the imine **5a**, for example, showed clearly different absorptions related to the enamine tautomers **4a**, namely a doublet at  $\delta_{\text{H}}$  3.56 ppm ( $^2J_{\text{PH}} = 15.2$  Hz) for the methylene protons as well as a high-field signal for the methyl group at 1.90 ppm, while in the  $^{13}\text{C-NMR}$  spectrum the absorption of methylene carbon is shifted to higher field ( $\delta_{\text{C}}$  45.2 ppm) with a lower value of the phosphorus-carbon coupling constant ( $^1J_{\text{PC}} = 62.2$  Hz) relative to those to the *E*- and *Z*-enamines **4a**.



Scheme 3

Table 1. Preparation of phosphine oxides **4/5** and phosphonium salts **7**.

Entry	Compound	R <sup>1</sup>	R <sup>2</sup>	Yield (%) <sup>a</sup>	E / Z ratio <sup>b</sup>	m.p. (°C)
1	<b>4/5a</b>	H	H	76	5/10/85 <sup>c</sup>	117-119
2	<b>4/5b</b>	H	Me	78	5/10/85 <sup>c</sup>	120-122
3	<b>7a</b>	H	H	91	100/0	175-176
4	<b>7b</b>	4,5-(MeO) <sub>2</sub>	H	92	100/0	207-209(d)

<sup>a</sup> Yield of isolated purified product. <sup>b</sup>E / Z ratio determined by <sup>31</sup>P-NMR. <sup>c</sup>E-4 / Z-4 / 5 determined by <sup>31</sup>P-NMR.

Formation of aminoquinolines **1** were observed when a mixture of the *Z*- and *E*-enamines **4** and the imine-tautomers **5** was used as starting material. Treatment of functionalized phosphine oxides **4/5** with a base such as sodium hydride led to the formation of aminoquinolinylphosphine oxides **1** (Scheme 3) in excellent yield (Table 2, entries 1-3). Spectroscopic data were in agreement with the assigned structure. Mass spectrometry of **1a** showed the molecular ion peak (*m/z* 358, 100 %), while the methyl group gave a <sup>1</sup>H resonance at  $\delta_H$  2.00 ppm. The formation of substituted quinolines **1** can be assumed to proceed *via* nucleophilic attack of the enamine carbon to the electrophilic nitrile group bonded to the aromatic ring. Compounds **1** can also be obtained in "one pot" reaction from the allenes **3** when the mixture of **4** and **5** were directly treated with sodium hydride.

Table 2. Preparation of 4-aminoquinolines **1**, **9** and **12** and iminoquinolines **10**.

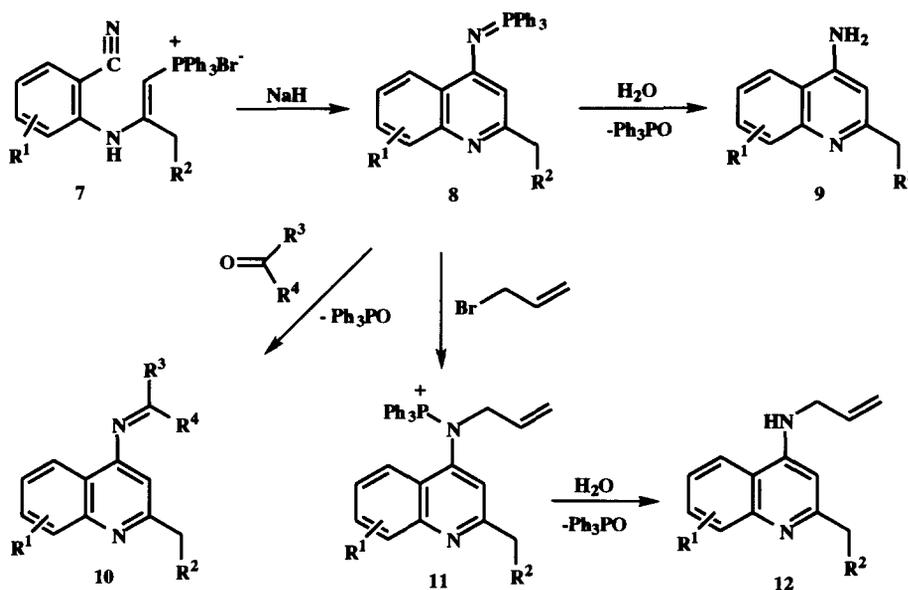
Entry	Comp.	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	Yield (%)	m.p. (°C)
1	<b>1a</b>	H	H			78 <sup>a</sup> (71) <sup>b</sup>	135-136
2	<b>1b</b>	6,7-(MeO) <sub>2</sub>	H			79 <sup>b</sup>	216-217
3	<b>1c</b>	H	Me			78 <sup>a</sup>	180-181
4	<b>9</b>	H	H			72 <sup>c</sup>	163-165 <sup>f</sup>
5	<b>10a</b>	H	H	<i>p</i> -Me-Ph	H	81 <sup>d</sup>	98-100
6	<b>10b</b>	H	H	CO <sub>2</sub> Et	CO <sub>2</sub> Et	77 <sup>d</sup>	oil <sup>g</sup>
7	<b>10c</b>	6,7-(MeO) <sub>2</sub>	H	3,4-(MeO) <sub>2</sub> -Ph	H	73 <sup>d</sup>	119-121
8	<b>12</b>	H	H			86 <sup>e</sup>	oil <sup>g</sup>

<sup>a</sup> Yield of isolated product **1** based on **4/5**. <sup>b</sup> Yield of isolated product **1** in "one pot" reaction from **3**. <sup>c</sup> Yield of isolated product **9** based on **7**. <sup>d</sup> Yield of isolated product **10** based on **7**. <sup>e</sup> Yield of isolated product **12** from **11**. <sup>f</sup> **9**: 167-169<sup>17</sup>. <sup>g</sup> Purified by flash chromatography.

#### Synthesis of 4-aminoquinolines **9** and **12** and iminoquinolines **10**.

This methodology used for the preparation of aminoquinolines **1** can also be applied to the synthesis of 4-aminoquinolines **9** when enamines derived from phosphonium salts **7** were used. Thus, addition of *o*-aminobenzonitriles, to commercially available propargyl phosphonium bromide<sup>18</sup> **6** in refluxing of

acetonitrile (TLC control) led to the exclusive formation of *E*- $\beta$ -enamino phosphonium salts **7** in excellent yield (Scheme 3, Table 1, entries 3-4). Compounds **7** were characterized by their spectroscopic data.



Scheme 4

Treatment of enamines derived from phosphonium salts **7** with sodium hydride gave 4-aminoquinolines **9**. Formation of quinolines **9** could be explained (Scheme 4) through intramolecular nucleophilic attack to the carbon-nitrogen triple bond of phosphorane generated "in situ" from  $\beta$ -enamino phosphonium salts **7** leading to phosphazene **8** in a similar way to that reported for the intermolecular reaction,<sup>12</sup> hydrolysis of which gave aminoquinoline **9**. Phosphazene intermediates **8**, previously postulated and not detected,<sup>17</sup> proved to be unstable to both distillation and chromatography and were not isolated, but the formation of these compounds in the crude reaction mixture was followed by NMR (<sup>1</sup>H, <sup>13</sup>C, <sup>31</sup>P). Additionally, the presence of phosphazenes **8** in the crude reaction mixture was confirmed when they were used "in situ" in aza-Wittig reactions and alkylation processes.<sup>11</sup> Reaction of compounds **8** with carbonyl derivatives such as *p*-tolualdehyde, veratraldehyde and diethyl ketomalonate in THF at room temperature gave imino compounds **10** derived from 4-aminoquinolines, while treatment of phosphazene **8** with allyl bromide led to the formation of the aminophosphonium salt **11**, hydrolysis of which gave *N*-substituted 4-aminoquinoline **12**.

In conclusion, we describe an easy and efficient method for the synthesis of 4-aminoquinolines substituted with a phosphine oxide **1** in the 3-position, and 4-aminoquinolines **9** and **12** from readily available starting materials such as *o*-aminobenzonitriles and allenes (see Scheme 2) 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>1-6</sup>

## ACKNOWLEDGEMENTS

The present work has been supported by the Dirección General de Investigación Científica y Técnica (DGICYT, PB96-0252) and by the Departamento de Educación, Universidades e Investigación del Gobierno (GV, PI-96/36). J. García thanks the Ministerio de Educación y Ciencia for a Predoctoral Fellowship.

## EXPERIMENTAL SECTION

**General.** Melting points were determined with a Buchi SPM-20 apparatus and are uncorrected. Analytical *TLC* was performed on 0.25 mm silica gel plates (Merck). Visualization was accomplished by *UV* light and iodine. All solvents used in reactions were freshly distilled from appropriate drying agents before use: *THF* (sodium benzophenone ketyl) acetonitrile ( $P_2O_5$ ); chloroform ( $P_2O_5$ ). 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.  $^1H$ -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  $CDCl_3$  solutions.  $^{13}C$ -NMR spectra were recorded at 75 MHz with chloroform (77.0 ppm) as an internal reference in  $CDCl_3$  solutions.  $^{31}P$ -NMR spectra were recorded at 120 MHz with 85% phosphoric acid as an external reference. Elemental analyses were performed in a Leco CHNS-932 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  $cm^{-1}$ . 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  $N_2$ .

### General Procedure for the Preparation of the $\beta$ -Enamino 4 - and/or $\beta$ -Iminophosphine Oxides 5.

A dry flask, 100-ml, 2-necked, fitted with a dropping funnel, gas inlet, and magnetic stirrer, was charged with 1.2 g (5 mmol) of allenediphenylphosphine oxide<sup>15</sup> **3** ( $R^2=H$ ), or 1.27 g (5 mmol) of 1,2-butadienyldiphenylphosphine oxide<sup>15</sup> **3** ( $R^2 = CH_3$ ), and 25 mL of acetonitrile. A solution (5 mmol) of amine and 10 mL of acetonitrile was added over 10 min. The mixture was stirred and refluxed until *TLC* indicated the disappearance of the phosphine oxide **3** (48 h). The mixture was concentrated and the crude product was purified by recrystallization (hexane /  $CH_2Cl_2$ ).

**Z - and E- $\beta$ -N-o-Cyanophenylaminoprop-1-enyldiphenylphosphine oxide (4a) and  $\beta$ -N-o-cyanophenyliminopropyl-diphenylphosphine oxide (5a).** 1360 mg (76 %) of **4a/5a** as a white solid. Data for **4a**: mp 116-118 °C;  $^1H$ -NMR (300 MHz) **4a**: 2.03 and 2.19 (s, 3H, *E*- and *Z*- $CH_3$ ), 3.67 (s, 1H, NH), 4.18 (d, 1H,  $^2J_{PH}= 22.2$  Hz, *Z*-CH), 5.02 (d, 1H,  $^2J_{PH}= 17.7$  Hz, *E*-CH), 6.29-7.76 (m, 14H, arom). **5a**: 1.90 (s, 3H,  $CH_3$ ), 3.56 (d, 2H,  $^2J_{PH}= 15.2$  Hz,  $CH_2$ -P), 6.29-7.76 (m, 14H, arom);  $^{13}C$ -NMR (75 MHz) **4a**: 19.9 (d,  $^3J_{PC}= 14.7$  Hz, *Z*- $CH_3$ ), 23.2 (d,  $^3J_{PC}= 5.4$  Hz, *E*- $CH_3$ ), 77.2 (d,  $^1J_{PC}= 114.2$  Hz, *Z*-C-P), 81.0 (d,  $^1J_{PC}= 128.8$  Hz, *E*-C-P), 110.1-136.1 (C-arom and CN), 156.7 (=C-N). **5a**: 21.3 ( $CH_3$ ), 45.2 (d,  $^1J_{PC}= 62.2$  Hz,  $CH_2$ -P), 110.1-136.1 (C-arom and CN), 165.2 (=C-N);  $^{31}P$ -NMR (120 MHz). **4a**: 25.6 (*E*-isomer), 29.7 (*Z*-

isomer). **5a**: 28.8; *IR* (*KBr*) 3190, 3152, 2227, 1521, 1177  $\text{cm}^{-1}$ ; *MS* (EI) 358 ( $\text{M}^+$ , 10). Anal. Calcd for  $\text{C}_{22}\text{H}_{19}\text{N}_2\text{OP}$ : C, 73.74; H, 5.31; N, 7.82. Found: C, 73.66; H, 5.36; N, 7.75.

**Z- and E- $\beta$ -N-o-Cyanophenylaminobut-1-enyldiphenylphosphine oxide (4b) and  $\beta$ -N-o-cyanophenyliminobutyl-diphenylphosphine oxide (5b)**. 1451 mg (78 %) of **4b/5b** as a white solid. Data for **4b**: mp 124–126  $^{\circ}\text{C}$ ;  $^1\text{H-NMR}$  (300 MHz) **4b**: 1.03 and 1.06 (t, 3H,  $^3J_{\text{HH}}=7.1$  Hz, *E*- and *Z*- $\text{CH}_3$ ), 2.29–2.44 (m, 2H,  $\text{CH}_2$ ), 4.33–4.87 (m, 2H, NH and *E*- and *Z*-CH), 6.29–7.91 (m, 15H, arom). **5b**: 0.98 (t, 3H,  $^3J_{\text{HH}}=7.0$  Hz,  $\text{CH}_3$ ), 2.62 (q, 2H,  $^3J_{\text{HH}}=7.0$  Hz,  $\text{CH}_2$ ), 3.42 (d, 2H,  $^2J_{\text{PH}}=14.8$  Hz,  $\text{CH}_2\text{-P}$ ), 6.29–7.91 (m, 15H, arom);  $^{13}\text{C-NMR}$  (75 MHz) **4b**: 10.6 and 12.1 ( $\text{CH}_3$ ), 28.4 ( $\text{CH}_2$ ), 78.0 (d,  $^1J_{\text{PC}}=113.7$  Hz, *Z*-CH), 81.2 (d,  $^1J_{\text{PC}}=129.2$  Hz, *E*-CH), 110.2–132.1 (C-arom and CN), 159.0 (=C-N). **5b**: 7.9 ( $\text{CH}_3$ ), 27.1 ( $\text{CH}_2$ ), 48.2 (d,  $^1J_{\text{PC}}=61.6$  Hz,  $\text{CH}_2\text{-P}$ ), 110.2–132.1 (C-arom and CN), 167.7 (C=N);  $^{31}\text{P-NMR}$  (120 MHz) **4b**: 25.9 (*E*-isomer), 30.0 (*Z*-isomer). **5b**: 28.1; *IR* (*KBr*) 3230, 3143, 2213, 1523, 1221  $\text{cm}^{-1}$ ; *MS* (EI) 372 ( $\text{M}^+$ , 33). Anal. Calcd for  $\text{C}_{24}\text{H}_{21}\text{N}_2\text{OP}$ : C, 77.42; H, 5.65; N, 7.53. Found: C, 77.56; H, 5.72; N, 7.65.

**General Procedure for the Preparation of the  $\beta$ -Aminoprop-1-enylphosphonium Bromides 7.** A dry flask, 100-ml, 2-necked, fitted with a dropping funnel, gas inlet, and magnetic stirrer, was charged with 1.9 g (5 mmol) of propargyltriphenylphosphonium bromide **6** and 25 mL of acetonitrile. A solution (5 mmol) of amine and 10 mL of acetonitrile was added over 10 min. The mixture was stirred and refluxed until *TLC* indicated the disappearance of phosphonium salt (48 h). The mixture was concentrated and the crude product was triturated with diethyl ether.

**E- $\beta$ -N-o-Cyanophenylaminoprop-1-enylphosphonium bromide (7a)**. 2270 mg (91 %) of **7a** as a white solid. Data for **7a**: mp 175–176  $^{\circ}\text{C}$ ;  $^1\text{H-NMR}$  (300 MHz) 2.09 (s, 3H,  $\text{CH}_3$ ), 4.15 (d, 1H,  $^2J_{\text{PH}}=14.8$  Hz, CH), 7.31–7.98 (m, 19H, arom), 10.72 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 21.5 ( $\text{CH}_3$ ), 63.5 (d,  $^1J_{\text{PC}}=118.8$  Hz, CH), 109.6–140.4 (C-arom and CN), 163.9 (=C-N);  $^{31}\text{P-NMR}$  (120 MHz) 16.9; *IR* (*KBr*) 3138, 2985, 2220, 1514, 1242, 1103  $\text{cm}^{-1}$ ; *MS* (EI) 418 ( $\text{M}^+\text{-HBr}$ , 19). Anal. Calcd for  $\text{C}_{28}\text{H}_{24}\text{N}_2\text{PBr}$ : C, 67.33; H, 4.81; N, 5.61. Found: C, 67.41; H, 4.79; N, 5.76.

**E- $\beta$ -N-2-Cyano-4,5-dimethoxyphenylaminoprop-1-enylphosphonium bromide (7b)**. 2570 mg (92 %) of **7b** as a yellow solid. Data for **7b**: mp 207–209  $^{\circ}\text{C}$ ;  $^1\text{H-NMR}$  (300 MHz) 2.06 (s, 3H,  $\text{CH}_3$ ), 3.88 (s, 3H,  $\text{CH}_3\text{-O}$ ), 3.98 (s, 3H,  $\text{CH}_3\text{-O}$ ), 4.20 (sbroad, 1H, CH-P), 6.99–7.77 (m, 17H, arom), 10.52 (s, 1H, NH);  $^{13}\text{C-NMR}$  (75 MHz) 21.4 ( $\text{CH}_3$ ), 55.9 ( $\text{CH}_3\text{-O}$ ), 56.1 ( $\text{CH}_3\text{-O}$ ), 62.9 (d,  $^1J_{\text{PC}}=119.3$  Hz, CH-P), 100.2–153.3 (C-arom and CN), 163.6 (=C-N);  $^{31}\text{P-NMR}$  (120 MHz) 16.8; *IR* (*KBr*) 3409, 2932, 2210, 1513, 1093  $\text{cm}^{-1}$ ; *MS* (EI) 478 ( $\text{M}^+\text{-HBr}$ , 13). Anal. Calcd for  $\text{C}_{30}\text{H}_{28}\text{N}_2\text{O}_2\text{PBr}$ : C, 64.40; H, 5.01; N, 5.02. Found: C, 64.51; H, 5.13; N, 4.93.

**General Procedure for the Preparation of the 4-Aminoquinolines 1.** A dry flask, 100-ml, 2-necked, fitted with a dropping funnel, gas inlet, and magnetic stirrer, was charged with NaH (3 mmol) and  $\text{CHCl}_3$  (20 mL). A solution of a mixture of  $\beta$ -enaminophosphine oxides **4** and  $\beta$ -iminophosphine oxides **5** (3 mmol) in  $\text{CHCl}_3$  (10 mL) was then added. The mixture was stirred and refluxed until *TLC* indicated the disappearance of the compounds **4/5**. The mixture was diluted with water (30 mL) and extracted with  $\text{CH}_2\text{Cl}_2$  (3 x 15 mL). The  $\text{CH}_2\text{Cl}_2$  layers were washed with water (2 x 20 mL). The combined organic layers were dried over  $\text{MgSO}_4$ , filtered, and concentrated. The crude product was purified by flash-chromatography on silica gel (hexane/ethyl acetate, 1/1). Quinolines can also be obtained in "one pot" reaction: A solution of 3 mmol of allenes **3** and *o*-aminobenzonitrile **2** in acetonitrile was stirred and refluxed (~3 days), treated with NaH and heated until formation of **1** (*TLC* control). The quinoline **1** was purified as described above.

**3-Diphenylphosphoryl-2-methyl-4-aminoquinoline (1a).** 795 mg (78 %) of **1a** as a white solid. Data for **1a**: mp 135–136 °C;  $^1\text{H-NMR}$  (300 MHz) 2.00 (s, 3H, CH<sub>3</sub>), 7.42–7.86 (m, 16H, arom and NH<sub>2</sub>);  $^{13}\text{C-NMR}$  (75 MHz) 28.4 (CH<sub>3</sub>), 95.4 (d,  $^1J_{\text{PC}} = 102.8$  Hz, C-P), 117.4–159.3 (C-arom);  $^{31}\text{P-NMR}$  (120 MHz) 40.1; *IR* (KBr) 3430, 3350, 3024, 1646, 1217 cm<sup>-1</sup>; *MS* (EI) 358 (M<sup>+</sup>, 74). Anal. Calcd for C<sub>22</sub>H<sub>19</sub>N<sub>2</sub>O<sub>3</sub>P: C, 73.74; H, 5.31; N, 7.82. Found: C, 73.67; H, 5.46; N, 7.73.

**3-Diphenylphosphoryl-2-methyl-6,7-dimethoxy-4-aminoquinoline (1b).** 990 mg (79 %) of **1b** as a white solid. Data for **1b**: mp 216–217 °C;  $^1\text{H-NMR}$  (300 MHz) 1.92 (s, 3H, CH<sub>3</sub>), 3.86 (s, 3H, CH<sub>3</sub>), 3.97 (s, 3H, CH<sub>3</sub>), 6.31–8.12 (m, 14H, arom and NH<sub>2</sub>);  $^{13}\text{C-NMR}$  (75 MHz) 29.5 (CH<sub>3</sub>), 55.2 (CH<sub>3</sub>), 55.8 (CH<sub>3</sub>), 100.1 (d,  $^1J_{\text{PC}} = 107.0$  Hz, C-P), 117.9–159.9 (C-arom);  $^{31}\text{P-NMR}$  (120 MHz) 40.0; *IR* (KBr) 3370, 3191, 1640, 1440, 1150 cm<sup>-1</sup>; *MS* (EI) 418 (M<sup>+</sup>, 30). Anal. Calcd for C<sub>24</sub>H<sub>23</sub>N<sub>2</sub>O<sub>3</sub>P: C, 68.90; H, 5.50; N, 6.70. Found: C, 69.02; H, 5.58; N, 6.61.

**3-Diphenylphosphoryl-2-ethyl-4-aminoquinoline (1c).** 870 mg (78 %) of **1c** as a white solid. Data for **1c**: mp 180–181 °C;  $^1\text{H-NMR}$  (300 MHz) 0.55 (t, 3H,  $^3J_{\text{HH}} = 7.2$  Hz, CH<sub>3</sub>), 2.36 (q, 3H,  $^3J_{\text{HH}} = 7.2$  Hz, CH<sub>2</sub>), 7.26–7.87 (m, 16H, arom and NH<sub>2</sub>);  $^{13}\text{C-NMR}$  (75 MHz) 12.6 (CH<sub>3</sub>), 33.1 (CH<sub>2</sub>), 94.8 (d,  $^1J_{\text{PC}} = 103.2$  Hz, C-P), 117.3–163.7 (C-arom);  $^{31}\text{P-NMR}$  (120 MHz) 40.5; *IR* (KBr) 3383, 3218, 2953, 1639, 1229 cm<sup>-1</sup>; *MS* (EI) 372 (M<sup>+</sup>, 47). Anal. Calcd for C<sub>23</sub>H<sub>21</sub>N<sub>2</sub>O<sub>3</sub>P: C, 74.19; H, 5.64; N, 7.53. Found: C, 74.08; H, 5.51; N, 7.61.

**Reaction of phosphonium salts 7 with sodium hydride.** Sodium hydride (3 mmol) was added to a solution of phosphonium salts **7** (3 mmol) in acetonitrile (20 mL). The reaction mixture was refluxed and stirred under nitrogen for 3 days to give the phosphazenes **8**. The reaction product is unstable to distillation or chromatography and therefore was not isolated and used for the following reactions, without further purification.

**2-Methyl-4-triphenylphosphoiminoquinoline 8a.** Data for **8a**:  $^1\text{H-NMR}$  (300 MHz) of crude reaction mixture: 2.11 (s, 3H, CH<sub>3</sub>), 6.33–7.90 (m, 14H, arom);  $^{13}\text{C-NMR}$  (75 MHz) of crude reaction mixture: 28.7 (CH<sub>3</sub>), 115.0–161.3 (C-arom);  $^{31}\text{P-NMR}$  (120 MHz) 14.7.

**2-Methyl-6,7-dimethoxy-4-triphenylphosphoiminoquinoline 8b.** Data for **8b**:  $^1\text{H-NMR}$  (300 MHz) of crude reaction mixture: 1.99 (s, 3H, CH<sub>3</sub>), 3.79 (s, 3H, CH<sub>3</sub>-O), 3.84 (s, 3H, CH<sub>3</sub>-O), 6.77–7.83 (m, 14H, arom);  $^{13}\text{C-NMR}$  (75 MHz) of crude reaction mixture: 28.5 (CH<sub>3</sub>), 55.9 (CH<sub>3</sub>-O), 56.5 (CH<sub>3</sub>-O), 118.1–154.3 (C-arom);  $^{31}\text{P-NMR}$  (120 MHz) 14.2.

**Aza-Wittig reaction of *N*-quinolinyl phosphazenes 8 with carbonyl compounds. Synthesis of iminoquinolines 10.** A solution of carbonyl compounds (3 mmol) in anhydrous THF (20 mL) was added dropwise to a solution of phosphazene **8** generated "in situ" from β-enaminophosphonium bromide **7**. The mixture was stirred at room temperature until TLC indicated the disappearance of phosphazene **8**. 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).

**Syn- and anti-2-methyl-4-(*p*-methylphenylimino)quinoline 10a.** 632 mg (81 %) of **10a** as a yellow solid. Data for **10a**: mp 98–100 °C;  $^1\text{H-NMR}$  (300 MHz) 2.10 and 2.34 (s, 3H, CH<sub>3</sub>), 2.38 and 2.52 (s, 3H, CH<sub>3</sub>), 6.40–7.83 (m, 10H, arom and H-C=N);  $^{13}\text{C-NMR}$  (75 MHz) 16.7 (CH<sub>3</sub>), 21.4 (CH<sub>3</sub>), 117.3–154.5 (C-arom), 167.5 and 168.6 (C=N); *IR* (KBr) 3038, 2979, 1630, 1222 cm<sup>-1</sup>; *MS* (EI) 260 (M<sup>+</sup>, 32). Anal. Calcd for C<sub>18</sub>H<sub>16</sub>N<sub>2</sub>: C, 83.08; H, 6.15; N, 10.78. Found: C, 83.19; H, 6.21; N, 10.87.

**Syn- and anti-2-methyl-4-(diethoxycarbonylimino)quinoline 10b.** 725 mg (77 %) of **10b** as a yellow oil. Data for **10b**:  $R_f = 0.80$  (ethyl acetate);  $^1H-NMR$  (300 MHz) 1.16–1.34 (m, 6H,  $CH_3$ ), 1.94 and 2.04 ( $CH_3$ ), 5.90 and 5.93 (s, 1H,  $C_3-H$ ), 6.74–7.62 (m, 4H, arom);  $^{13}C-NMR$  (75 MHz) 13.8 and 14.0 ( $CH_3$ ), 18.4 and 20.6 ( $CH_3$ ), 59.2 and 62.0 ( $CH_2$ ), 118.0–152.6 (C-arom), 167.4 and 168.2 (C=O), 173.2 (C=N);  $IR$  (KBr) 3162, 2972, 1730, 1273  $cm^{-1}$ ;  $MS$  (EI) 314 ( $M^+$ , 56). Anal. Calcd for  $C_{17}H_{18}N_2O_4$ : C, 64.97; H, 5.73; N, 8.92. Found: C, 64.88; H, 5.61; N, 9.03.

**Syn- and anti-2-methyl-6,7-dimethoxy-4-(3,4-dimethoxyphenylimino)quinoline 10c.** 801 mg (73 %) of **10c** as a yellow solid. Data for **10c**: mp 119–121;  $^1H-NMR$  (300 MHz) 2.13 and 2.49 (s, 3H,  $CH_3$ ), 3.87, 3.89, 3.90 and 3.91 (s, 3H,  $CH_3-O$ ), 6.38 (s, 1H,  $C_3-H$ ), 6.84–7.77 (m, 7H, arom and H-C=N);  $^{13}C-NMR$  (75 MHz) 16.2 and 22.8 ( $CH_3$ ), 55.4, 55.5, 55.6, 55.7 and 55.9 ( $CH_3-O$ ), 110.2–153.0 (C-arom), 167.5 and 168.7 (C=N);  $IR$  (KBr) 2959, 1595, 1508, 1260  $cm^{-1}$ ;  $MS$  (EI) 366 ( $M^+$ , 36). Anal. Calcd for  $C_{21}H_{22}N_2O_4$ : C, 68.85; H, 6.01; N, 7.65. Found: C, 68.96; H, 6.11; N, 7.58.

**Reaction of phosphazene 8a with allyl bromide. Synthesis of N-allyl-N-(2-methyl-4-aminoquinolinyl)phosphonium bromide 11.** Allyl bromide (3 mmol) was added to a solution in acetonitrile (20 mL) of phosphazene **8a** generated "in situ" from  $\beta$ -enaminophosphonium bromide **7a**. The mixture was stirred until  $^{31}P-NMR$  indicated the disappearance of phosphazene. The mixture was concentrated and the crude product was triturated with diethyl ether to afford 1358 mg (84%) of **11** as a yellow solid. Data for **11**: mp 214–217 °C;  $^1H-NMR$  (300 MHz) 2.53 (s, 3H,  $CH_3$ ), 4.86–5.30 (m, 4H, = $CH_2$  and N- $CH_2$ ), 6.13 (m, 1H, =CH), 7.29–8.91 (m, 20H, arom);  $^{13}C-NMR$  (75 MHz) 22.6 ( $CH_3$ ), 51.4 ( $CH_2-N$ ), 109.7 (d,  $^3J_{PC} = 12.8$  Hz, =CH), 117.5 (=CH<sub>2</sub>), 125.1–164.2 (C-arom);  $^{31}P-NMR$  (120 MHz) 16.5;  $IR$  (KBr) 3436, 3045, 1587, 1487, 1441  $cm^{-1}$ ;  $MS$  (EI) 458 ( $M^+ - HBr$ , 15). Anal. Calcd for  $C_{31}H_{28}N_2PBr$ : C, 69.01; H, 5.19; N, 5.20. Found: C, 69.13; H, 5.02; N, 5.31.

**Synthesis of 2-methyl-4-allylaminoquinoline 12. Hydrolysis of N-allyl-N-(2-methyl-4-aminoquinolinyl)phosphonium bromide 11.** A 1 M aqueous solution of HCl (10 mL) was added to a solution of **11** (1078 mg, 2 mmol) in methanol (20 mL). The mixture was stirred until  $TLC$  indicated the disappearance of compound **11** (12 h). The mixture was diluted with water (30 mL) and extracted with  $CH_2Cl_2$  (3 x 20 mL). The  $CH_2Cl_2$  layers were washed with water (2 x 20 mL). The combined organic layers were dried over  $MgSO_4$ , filtered and concentrated to afford an oil that was chromatographed on silica gel to give 321 mg (81%) of **12** as a yellow oil ( $R_f = 0.2$ , ethyl acetate). Data for **12**:  $^1H-NMR$  (300 MHz) 2.57 (s, 3H,  $CH_3$ ), 3.71 (m, 2H, N- $CH_2$ ), 4.98–5.21 (m, 3H, =CH and  $CH_2$ ), 6.17 (s, 1H, NH), 6.53 (s, 1H,  $C_3-H$ ), 7.40–7.95 (m, 4H, arom);  $^{13}C-NMR$  (75 MHz) 29.6 ( $CH_3$ ), 53.8 ( $CH_2-N$ ), 103.2–161.9 (C-arom);  $IR$  (KBr) 3415, 3002, 1440, 1277  $cm^{-1}$ ;  $MS$  (EI) 198 ( $M^+$ , 35). Anal. Calcd for  $C_{13}H_{14}N$ : C, 78.79; H, 7.07; N, 7.08. Found: C, 78.87; H, 7.15; N, 6.90.

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